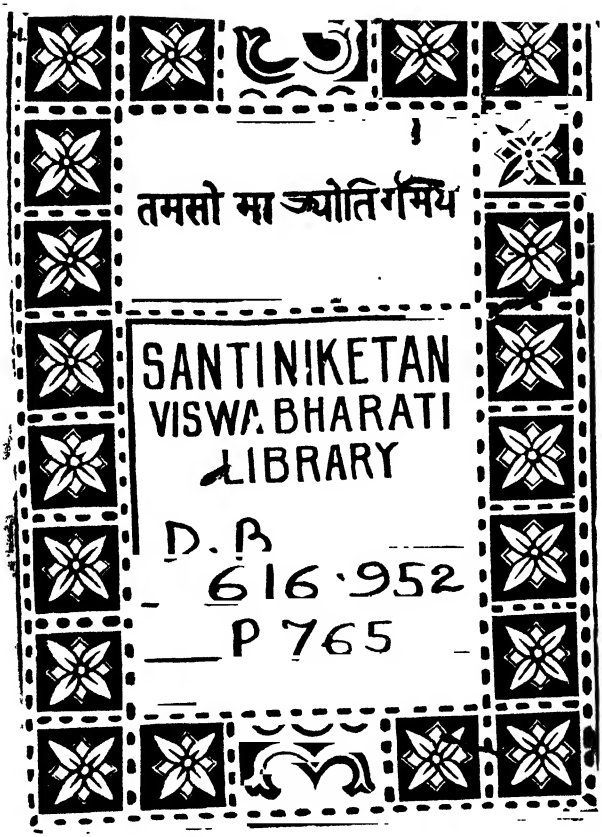
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GONOCOCCAL INFECTIONS

OXFORD MEDICAL PUBLICATIONS

GONOCOCCAL INFECTIONS

BY

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PREFACE

In the following pages we have endeavoured to give a concise account of the present state of our knowledge of this important subject.

The reader who has made a special study of these diseases will find little that is new in what we have written, but we trust that our work will be of use to those who wish to gain a practical general knowledge of gonococcal infections.

INTRODUCTION

Up till a few years ago almost the only recognized gonococcal infection was gonorrhoea with a few of its commoner complications, e.g. epididymitis, arthritis and ophthalmia. That a gonococcal infection should be regarded as a serious disease which might lead to permanent deformity, cause loss of life and even affect the national welfare by diminishing the birth rate, was never seriously considered, much less thought worthy of scientific investigation. In fact, the general attitude of the medical profession towards gonorrhoea might well have been summed up in the answer of the Irish medical student who, when asked how he would treat gonorrhoea, replied "with contimpt."

This attitude resulted from ignorance of the serious nature of the disease, coupled with a puritanical prejudice against the patient, who was

looked on as merely suffering some temporary discomfort—a well-merited punishment for his sin.

The subject has assumed an entirely new aspect, thanks to the investigations of Neisser, Finger and many others, who have demonstrated the serious consequences which may ensue, not only to the patient himself but to his wife and offspring as the result of a gonococcal infection.

Neisser's discovery of the gonococcus marked an immense advance in our knowledge of these infections. Previous to this the diagnosis of a gonococcal infection was mainly a matter of guess-work and only possible when the symptoms had become more or less fully developed. The early diagnosis of a gonococcal infection of important parts, such as the conjunctiva, was impossible, with the result that in most cases the part was seriously damaged owing to the delay in commencing treatment. Again, when the actual cause of the disease was unknown treatment was entirely directed to allaying the accompanying symptom of inflammation, the

disease being meanwhile allowed to establish itself firmly in the tissues.

In regard to the pathology of gonococcal infections our knowledge has made great strides, for in addition to the causal germ we now know many if not all the changes which it produces in the tissues.

In spite of much patient research the treatment of gonococcal infections is still far from satisfactory. The newer organic compounds of silver have furnished us with an effective weapon for making a direct attack on the gonococcus when it occupies a superficial position on a mucous membrane, and the vaccine treatment has enabled us by making a flank attack to turn the gonococci out of certain previously unassailable positions in the body, but we must acknowledge that when they have established themselves in the epithelium of a mucous membrane they are able to defy any attack we may make on them; in other words we do not yet know how to cure a chronic gonorrhoea. Consequently the prognosis as regards elimination of the gonococci is by no means favourable; in fact,

the Vienna school teaches that every attack of gonorrhoea is curable except the first. This view is probably too pessimistic, though we must admit that when once the gonococcus has been allowed to obtain a firm foothold on a mucous membrane only a rash or inexperienced man would venture to predict when the mucous membrane would be entirely free from these micro-organisms, and as long as one pair of them retain their vitality, so long is there a possibility of future trouble.

If all persons were equally susceptible to the gonococcus we might confidently say that the prognosis depended almost entirely on whether the gonococci had been permitted to penetrate below the surface before treatment was begun. On an exposed surface, where a drug can be brought into contact with it, the resistance of the gonococcus is small and almost any kind of treatment is sufficient to destroy it and cure the patient. When the gonococci have been allowed to penetrate to the inter-epithelial spaces they are protected from the action of any drug applied to the surface of the mucous membrane and to

an almost equal extent from the action of any substance circulating in the blood. Once firmly established in these spots they are like the garrison of a bomb-proof fort, which in spite of a fierce attack from all sides, can go on quietly existing, ready to sally forth whenever a suitable occasion arrives.

When the disease has reached the chronic stage the gonococci may continue to exist in the inter-epithelial spaces and ducts of glands for years without giving rise to any noticeable symptoms. If, however, anything occurs to lower the vitality of the tissues in which the gonococci are residing or to supply them with more nourishment, as is done by increased vascularity of the mucous membrane, they will almost certainly again become active, begin to multiply rapidly and set up a fresh attack of the disease, though not quite so acute as the original one. This is very likely to occur in the case of a man who while harbouring gonococci in the quiescent state indulges in sexual intercourse, and more especially if he is under the influence of alcohol at the time. In

the married state the man may transfer some of his quiescent gonococci to his wife: the transference to a fresh soil may restore their virulence so that both husband and wife may become infected, resulting in much unhappiness and suffering.

The woman who is a sufferer from chronic gonorrhoea may unknowingly infect her child's eyes at birth, or in the case of a female child be the means of causing a gonococcal vulvo-vaginitis by attending to her with soiled fingers. Chronic gonorrhoea is unfortunately only too common; as it frequently gives rise to no symptoms the sufferer does not realize his or her position and is thus the means, in most cases innocently, of passing on the disease with all its dread possibilities. If it were in our power to prevent the occurrence of chronic gonorrhoea the incidence of the disease would speedily be reduced to an almost negligible quantity.

Another aspect in the prognosis of gonorrhoea and one which has hardly been sufficiently appreciated, at least by the general public, is its influence on the national birth rate.

Thus a man who has suffered from gonococcal epididymitis may as a result have his seminal tubules blocked and thus become incapable of impregnating his wife. Similarly in a woman the Fallopian tubes may be occluded as the result of a gonococcal inflammation, thus rendering her sterile. Chronic gonococcal endometritis may prevent fertilization of the ovum or lead to its expulsion at an early period of gestation. When, as not infrequently happens, the inflammation spreads to the structures around the uterus there may be, in addition to barrenness, intense suffering for years, with the result that the woman becomes a helpless invalid for the best part of her life.

One other point which must be remembered in the prognosis of gonococcal infections is that the inflammatory products of these infections tend to become converted into fibrous tissue instead of being absorbed. Thus stricture of the urethra, with all its attendant sequelae, or anchylosis of a joint may result from a gonococcal infection of the parts concerned.

The potential gravity of gonococcal infections

makes their prophylaxis a subject of the greatest importance. Gonococcal infections may be contracted: (1) By direct contact with an infected person, e.g. during connexion, or in the case of the child's eyes during parturition. (2) By contact with fingers, towels, etc., soiled with a gonococcal discharge. (3) While attending to patients suffering from a gonococcal infection.

The prophylaxis may conveniently be considered under the same three headings.

(1) **Sexual Connexion.**—The great majority of gonococcal infections are contracted during promiscuous sexual intercourse. If therefore persons of both sexes would practise continence till marriage, gonococcal infections would cease to take place and the disease would die out. Unfortunately this highly desirable state of affairs is not likely to take place in the near future.

As this work is not concerned with the moral aspects of free love it only remains to point out briefly that if a person chooses to indulge in sexual intercourse with an unknown person of the opposite sex, it is his or her duty,

if only for the sake of the community in general, to take such precautions as will be likely to prevent the acquisition of a gonococcal infection. This may be effected in the case of a male by using a mechanical protection, the well-known rubber condom, or by applying a gonococcicidal agent to the penis and meatus directly after completing the act. Unfortunately the men who consort with loose women will rarely take the trouble to make use of any prophylactic agent, even when these are provided for their protection, unless a certain amount of compulsion is employed. In the German Navy very good results were obtained by furnishing men going on shore with a tube containing 20 per cent. protargol solution in gelatine. The men were directed to wash the penis after connexion and then squeeze the contents of the tube into the meatus. In some ships of the American Navy all men returning from shore leave were made to report to the sick bay orderly, and if they had exposed themselves to infection were first made to wash the penis thoroughly with an antiseptic lotion, and then received an irrigation with potassium

permanganate or an injection of a 5 per cent. solution of protargol, the glans penis being finally rubbed over with a 30 per cent. calomel ointment. Among the cases in which this procedure was carried out there were no infections with any kind of venereal disease.

Colonel Mervin Maus, Medical Corps, U.S.A., made a number of experiments with different kinds of antiseptic preparations, and as a result of these came to the conclusion that an ointment containing 30 per cent. of calomel in animal fat is an efficient protection against all venereal disease when used as he directs, viz. the ointment is rubbed on to the glans penis and a small quantity introduced into the meatus, after which the penis is gently massaged.

A female who chooses to run the risk of contracting a gonococcal infection should, immediately after the act, douche the vagina with a mild antiseptic solution, such as permanganate of potassium 2½ grains to the pint, and then, using an ordinary glass urethral syringe with a rubber tube or catheter attached to its nozzle, introduce a syringeful of a 2 per cent. solution

of protargol high up into the vagina. The douching, if thoroughly carried out and at once, would probably be quite efficient.

(2) **Contact with Soiled Fingers, Towels, etc.**—The most important gonococcal infections which may be contracted by contact with infective matter on fingers or articles of toilet are ophthalmia and vulvo-vaginitis in little girls. Gonococcal ophthalmia in adults occurs in most cases in men suffering from gonorrhoea, and is due to infection of the conjunctivae by the man's own fingers. The importance of disinfecting his fingers after handling his penis must therefore be impressed on him.

Similarly in infants if the mother has a gonorrhoeal discharge her fingers may infect the child's eyes; if her condition is known or suspected she must be solemnly warned of the necessity of avoiding any risk to the child's eyes.

Ophthalmia may also be contracted by using a towel, bath sponge, etc., which has recently been used by some unscrupulous person to remove a gonorrhoeal discharge. The serious consequences which may result from any such criminal

carelessness must therefore be pointed out to any one having a gonococcal discharge.

Gonococcal vulvo-vaginitis of little girls is liable to occur in children's hospitals in virulent epidemic form, causing much suffering to the little patients and discredit to the management of the institution. Its prophylaxis is of such importance that it will be fully considered when discussing the subject.

(3) **Gonococcal Infections contracted while attending to Patients.**—Such infections are of somewhat rare occurrence; still in a certain number of cases medical men and nurses have contracted gonococcal ophthalmia in this way. When a patient is suffering from an obvious gonococcal infection professional men should know enough not to run any risks, but in confinement cases the woman may, unknown to her medical attendant, be suffering from a chronic gonorrhoea the discharge from which contains virulent gonococci. When irrigating a patient suffering from gonorrhoea a drop of pus may be splashed into the surgeon's eye; to prevent this from happening goggles should be worn.

The disinfection of clothing worn by patients suffering from gonorrhoea may be referred to here. Provided it is thoroughly dried before being sent to the laundry no special disinfection need be undertaken. If for any reason disinfection is considered to be necessary it should be carried out by steeping the underclothing in some disinfecting solution which does not coagulate albumen, in preference to putting it through the steam disinfector, as in the latter the albumen of the discharges is coagulated and thus firmly fixed in the clothing. In consequence its removal in the laundry becomes difficult and the attempt is usually given up, with the result that the garment soon assumes a repulsive appearance and has to be condemned.

CHAPTER I

THE PATHOLOGY OF GONOCOCCAL INFECTIONS

The Gonococcus — Discovery. — In 1879 Neisser called attention to the constant presence of a micro-organism in acute gonorrhoeal discharges which he called the gonococcus, and maintained that it was the cause of gonorrhoea. His discovery was confirmed a little later by Bumm (1885), who succeeded in inducing gonorrhoea in a human being by means of cultures of the same organism.

Morphology.—As seen in gonorrhoeal discharges the gonococcus is shaped like two coffee beans, or kidneys, with their flat, or concave, sides opposing one another. The average size of the complete diplococcus seen under these conditions and stained in the ordinary way is 0·8 μ by 0·6 μ, so that it is about the same

size as a staphylococcus. Occasionally tetrads are seen instead of this diplococcus formation, and chain formation sometimes occurs. Its method of division generally appears to be as follows:—Starting as two hemispheres, with flat opposing sides, the latter become more and more indented so that the space between them, at first a narrow oblong, becomes oval. The indentation increases till each hemisphere is divided into two, along a plane at right angles to that of the original line of division, and a tetrad is formed; the two pairs of diplococci thus formed separate from one another, and the cycle starts afresh.

Though it possesses these morphological characteristics when seen in pathological secretions, and departures from the types described are seldom seen, yet under artificial conditions, as when grown on culture media, and when allowed to stand in urine for some time, it is one of the most prone of all organisms to undergo degeneration. If a specimen from a 48-hour old culture be stained and examined, probably half the cocci will be found swollen, many to two or

three times their size under natural conditions, and to be stained much more faintly than the rest. This tendency of the gonococcus to degenerate under artificial conditions is a characteristic of some value in diagnosis, but one it shares with the meningococcus, a micro-organism which it resembles in most other respects.

Staining Properties.—In smears from pathological discharges, as well as from cultures, it can be demonstrated with ease by staining it with any of the ordinary aniline basic dyes; those most commonly used for this purpose are Loeffler's alkaline methylene blue, carbol-methylene blue, watery methylene blue (1 per cent.), carbol-thionin blue, and weak carbol-fuchsin (1 of strong carbol-fuchsin and 9 of water). It is sufficient to apply any of these for one minute to the film after the latter has been fixed by passing it three times through the flame in the ordinary way.

Many combinations of stains have been devised with the object of making the gonococcus more easily distinguishable from surrounding structures in specimens made from pathological

secretions. As will be mentioned in more detail later, one of the chief characteristics of the gonococcus is that it is most frequently found inside the pus cells of gonorrhoeal discharges, and it assists the search if a stain combination be used which dyes the gonococcus a different colour from the protoplasm of the cell in which it lies. The formulae of a few of the numerous mixtures which have been devised at one time and another with this object are detailed in the appendix, with directions for their use.

It is useful to stain a specimen of gonorrhoeal discharge, or other pathological secretion, by one of the above methods when we wish to search it rapidly for cocci, but, as none of them are diagnostic, if diplococci are found it is invariably necessary to stain another specimen by Gram's method before a diagnosis is given. The gonococcus is decolorized by Gram's method, and as nearly 96 per cent. of Gram-negative cocci which occur in discharges from the male urethra are gonococci, and the other 4 per cent. of Gram-negative cocci found in this place have not the characteristic shape and intracellular

habitat of the gonococcus, this property is of the greatest diagnostic value in dealing with discharges from this situation.

In staining a specimen by Gram's method it is necessary to spread the secretion as thinly and evenly as possible, and to observe certain time limits fairly closely. The specimen is fixed by passing it three times through the flame and stained for one minute in aniline-, or carbol-gentian violet,[1] the excess stain is removed with blotting paper, and the specimen treated for one minute with Lugol's solution (iodine 1, potassium iodide 2, distilled water 300); it is then dried with blotting paper and flooded repeatedly with absolute alcohol till a cloud of blue no longer rises on the addition

[1] Aniline-gentian violet is conveniently made as follows: Add 3 c.c. of aniline oil to 100 c.c. of distilled water, shake well and filter through moist filter paper; to the filtered aniline oil water made in this way add 10 per cent. of a saturated alcoholic solution of gentian violet, shake well and filter on to the specimen. As aniline-gentian violet must be freshly prepared every week, it is more convenient, and equally effective, to use carbol gentian violet, which keeps for weeks; this is made by adding 10 c.c. of a saturated alcoholic solution of gentian violet to 90 c.c. of 2½ per cent. carbolic acid solution.

of fresh alcohol. The last process should not take longer than two minutes, since some specimens of staphylococci are decolorized by longer application of alcohol. It is counter-stained with Bismarck brown, or weak carbol-fucksin (carbol-fuchsin 1, distilled water 9), washed with water, dried and examined. Gonococci stain brown or red, according to the counter-stain used, while Gram-positive cocci stain blackish purple.

Cultivation on Artificial Media.—The gonococcus is somewhat more difficult to cultivate artificially than most other pathogenic micro-organisms, chiefly because it will not grow on ordinary laboratory media and is very sensitive to changes in temperature and to the reaction of the medium. For successful culture it is necessary to enrich the medium with uncoagulated albumen, preferably from a human source. Space will not permit of our describing even a small proportion of the numerous media which have been advocated for the cultivation of gonococci, and we propose to mention only the more important here; some others are detailed in the appendix.

By almost universal consent the most successful medium is Wertheim's, which is prepared by mixing equal parts of human serum and 2 per cent. nutrient agar (after the latter has been melted and cooled to between 40°C. and 50°C.) and preparing slopes, or plates, from the mixture. In place of human serum, many workers use ascitic, pleuritic, hydrocele or ovarian fluid, and these are very successful when rich in albumin. Of the above-mentioned human albuminous fluids we have had the most successful results from serum and pleuritic fluid, but failed to obtain any growth on a medium made with ascitic fluid which was rather poor in albumin.

It is easy to obtain human serum by bleeding from a vein at the bend of the elbow. A rubber band is fastened round the upper arm so as to retard the venous return without stopping the arterial flow. A prominent vein is selected, and the skin over it sterilized by painting it with a 1 in 15 solution of iodine (solid) in chloroform. A hollow needle is sterilized by immersion for a few minutes in oil which is heated till it just

smokes, picked out of the oil with sterile forceps and grasped at its middle with the right thumb and index finger, holding it so that it will enter the vein with its eye looking upwards. The blood is received into a sterile test-tube, which is held on the slope till replugged. When the clear serum separates it can be used at once or stored in sterile tubes.

To economize serum we pour a thin layer of the Wertheim's medium over the surface of a slope, or plate, of ordinary nutrient agar, to make a slab about a quarter of an inch thick on a foundation of plain agar.

The proper reaction of the agar is a question which is much debated, but one which it would not serve any useful purpose to discuss here, and we need only say that we have found a reaction of + 6 (Eyre's scale) uniformly successful.

Human blood can be mixed with agar in the same proportions, or a thin film of it can be spread over the surface of an ordinary nutrient agar slope. Gurd considers that haemoglobin is an advantage and advocates adding four to

seven drops of human blood to every 6 or 7 c.c. of ordinary nutrient agar made 0·6 per cent. acid to phenolphthalein, but we have found no additional advantage from the use of haemoglobin-containing fluids.

Blair Martin considers that the reaction is of prime importance and makes his medium as follows :—To an ordinary beef extract are added 0·5 per cent. of di-sodium phosphate (Na_2HPO_4), 1 per cent. of Witte's peptone and 2 per cent. of powdered agar; after heating in a Koch sterilizer, the medium is titrated while still hot, and made 0·6 per cent. acid to phenolphthalein with sodium hydrate. It is then sterilized in the usual way and slopes, or plates, are poured; in the case of slopes, three or four drops of serum, which has previously been heated at 57°C. for one and a half hours, are run over the surface, and the medium is incubated overnight to insure its sterility ; for plates, serum is added to the agar, after it has been melted and cooled to 45°C., in the proportion of 0·2 c.c. of serum to 5 c.c. of agar.

Of other media, including Wasserman's pig-

serum, nutrose agar and Finger's urine agar, we can only say they are apt to prove disappointing, and we advise the reader to carry out the first isolation, at any rate, on a medium made with human serum or human blood. After the gonococcus has been sub-cultured a few times on Wertheim's medium the proportion of human serum can be reduced to 1 of serum with 2 of agar.

Solid media for the cultivation of the gonococcus should always be fairly moist, and precautions taken accordingly to prevent evaporation during incubation and in store. This is best accomplished by fitting rubber caps over the plugs, and the caps may be reinforced with advantage by sealing again with melted paraffin.

The gonococcus will grow in serum broth, made by substituting ordinary nutrient broth for nutrient agar in Wertheim's medium, but fluid media are not so favourable to its growth.

The following is the simplest method of obtaining a pure culture of the gonococcus on Wertheim's medium or any of its modifications. A patient is chosen who is suffering from

acute gonorrhoea in the early stages and has not received any local treatment, and his glans penis is wiped over with a pledget of cotton wool soaked in absolute alcohol, which is kept applied for about a minute. Then, having warned the patient not to allow anything to touch his glans penis, a tube of the medium, which has previously been warmed to a temperature of 37°C. by keeping it in the incubator for an hour or so, is opened, and its surface dabbed all over with a platinum loop charged with secretion from the urethra. The secretion is obtained either by gently squeezing the urethra from without or by inserting the platinum loop a little distance along it. The tube is then plugged and capped, and at once transferred to the incubator. Though the gonococcus is not so sensitive to cold as to temperatures higher than 39°C. a greater percentage of successful cultures will result if the secretion be planted on warmed medium, and the latter placed in the incubator as soon as possible after inoculation. When the inoculation is made in the way we have described it is the exception not to obtain a pure culture.

When it is desired to obtain a culture from a case for diagnostic purposes, and there is reason to suspect the presence of other bacteria, the platinum loop charged with urethral secretion should be smeared over the surface of two or three slopes or plates in succession without recharging it. If the pathological material is bulky and probably contains few micro-organisms, as may happen in the case of joint fluid, a convenient plan is to melt some nutrient agar, allow it to cool to 40°C., mix with it an equal quantity of serum which has been heavily inoculated with the material and, after rapidly mixing, pour plates.

After twenty-four to thirty-six hours' incubation at 37°C. the colonies of gonococci appear as minute, greyish-white, semi-translucent dots, about the size of a small pin's head and resembling colonies of streptococci. The colonies do not increase greatly in size, but become slightly more heaped in the centre during the next few days. Surface colonies are round, with a wavy margin, while those below the surface are granular, with a regular margin. The growth is somewhat slimy

and sticks to the medium so closely that it is rather difficult to remove it without lifting some of the medium as well. The colonies do not run together in recently isolated cultures, but after subculturing for some months the growth may form a film covering the surface. When grown in a fluid medium it forms a granular pellicle on the surface or a deposit at the bottom of the tube, leaving the rest of the medium clear.

The gonococcus tends to die out somewhat rapidly if not subcultured frequently during the first few weeks after isolation, and the authors' practice is to transfer it to fresh medium every two days for the first fortnight and then to start cautiously, increasing the periods between the subcultures. After living under artificial conditions for a few months the period between the subcultures can be lengthened gradually to four or even six weeks, provided that the medium is kept moist. The gonococcus being very sensitive to drying, the tube should always be kept carefully sealed against evaporation with a rubber cap, or by paraffining the plug.

The cocci degenerate rapidly in cultures; if

an impression film be made by dropping a cover-slip on a colony and lifting it gently, and the resulting film be stained and examined it will be found that those cocci which have been removed from the centre of the colony are swollen to two or three times their normal size and stain feebly, and it is only those from the edge of the colony which have the normal size and shape. Whether degenerated cocci are dead or not it is impossible to say, since one cannot be sure of inoculating a medium with degenerated forms only. When regularly subcultured, the gonococcus can be kept alive indefinitely and eventually be induced to grow on ordinary nutrient agar, though the growth on this medium is always scanty and dies out very easily.

Vitality and Virulence.—As already stated, the gonococcus is very sensitive to changes in its environment, especially in regard to temperature and moisture. At 40°C. it dies in a few hours, however gradually the temperature may be raised. It is not quite so sensitive to cold, though growth ceases below 30°C., and we have succeeded in obtaining cultures from gonorrhoeal secretions

which have been kept in the ice-chest for twenty-four hours. It has been cultivated from infected towels and napkins which had been kept at room temperature for some hours, and Scholtz has cultivated it from infected bath water after twenty-four hours. In albuminous urine it appears to die out in twelve hours ; it cannot be recovered from non-albuminous urine after nine hours, and its staining properties disappear after eight hours in this medium. It is destroyed at once by drying.

With regard to the influence of chemicals, of those which are commonly used in the treatment of gonorrhoea, Schäffer and Steinschneider showed that silver nitrate in a strength of 1 in 4,000 killed it in ten minutes ; argentamin, 1 in 1,000, in five minutes ; protargol, 0·25 per cent., failed to exterminate it in ten minutes, though a 1 per cent. solution of the same chemical succeeded in the same time. Potassium permanganate in a strength of 1 in 1,000 failed to destroy it in ten minutes, and zinc sulphate, 1 in 400, was equally unsuccessful, but oxycyanate of mercury, 1 in 3,000, killed it in five minutes. Regarding the

action of other micro-organisms, Schäffer showed that gonococcus dies in the presence of B. pyocyaneus.

The above results are based on experiments *in vitro*, and their practical application to the therapeutics of gonococcal infections is unfortunately limited by some important factors, which may be shortly mentioned here. The gonococcus when growing under natural conditions is not so sensitive to rises of temperature; otherwise it would be a simple matter to cure gonorrhoea, or its complications, by artificially raising the patient's temperature to 40°C., for a day or two. Experience in this direction has, however, been disappointing. Finger failed to infect a few patients when they were suffering from fever, and some cases have been recorded in which spontaneous cure of gonorrhoea resulted from an attack of pyrexia, but generally, even though the rise of temperature be sustained for some days, its sole effect is to abate the discharge temporarily. With regard to the chemical agents we have mentioned, the difficulty is not so much the resistance of the

gonococcus as the fact that the antiseptic cannot penetrate sufficiently deeply to come into contact with it, and the same applies to pyocyanase, of which so much was hoped at first.

Notwithstanding its limitations from the point of view of therapeutics, a knowledge of the conditions which affect the vitality of the gonococcus is of considerable importance from that of hygiene, especially to those who are concerned with the care of little girls in institutions. The ease with which the vulvo-vaginitis of little girls, an affection which has been sufficiently proved to be gonorrhoeal in the great majority of cases, spreads through a ward shows the necessity of remembering that the gonococcus can remain alive and virulent on moist surfaces, as on towels and napkins, and in bath-water for many hours, and it is possible that if attention were paid to this and to the fact that complete drying destroys the infection, less would be heard of this scourge of children's institutions.

Diagnosis of Gonococci from other Organisms.—The gonococcus is easily distinguished

from the vast majority of other organisms by its coffee bean, or kidney, shape, its intracellular habitat and its behaviour to Gram's stain. In these respects, however, it resembles the meningococcus, M. catarrhalis and a few catarrhalis-like organisms which occur in the respiratory tract.

In dealing with male urethritis this resemblance is unimportant, since the latter organisms occur so very rarely in this situation that, for all practical purposes, reliance may be placed on microscopic characteristics only. In the female genital tract the diagnosis is rendered more difficult by the fact that a number of other Gram-negative diplococci occur, and it is not always easy to make out the characteristic shape of the gonococcus amongst the multitudes of other organisms which may be found in vaginal discharges. In addition to this, Gurd found M. catarrhalis four times in 113 examinations of vaginal discharge. In other situations than the genital tract it is always possible that one or other of the above organisms may be present. Thus in situations which communicate with the

respiratory tract, such as the conjunctiva, representatives of the catarrhalis group may be present, as well as the meningococcus, though the discovery of organisms having the microscopical characters and staining properties of the gonococcus in cases of acute purulent ophthalmia may be pretty safely accepted as proof of the gonococcal nature of the disease. Arthritis, endocarditis, and other metastatic affections which are often caused by gonococcal infections, may sometimes be due to the meningococcus, and the difficulty is increased by the fact that a meningococcal metastasis may exist without meningeal symptoms.

In all these cases recourse must be had to culture, by which the gonococcus can fairly easily be distinguished from the members of the catarrhalis group, though not so easily from the meningococcus. M. catarrhalis grows much more easily on media which are favourable to the gonococcus and can generally be cultivated on ordinary nutrient agar, as well as on gelatine. It is much less sensitive to changes in temperature and does not require

to be subcultured nearly so frequently as the gonococcus. The colonies of catarrhalis are opaque white and friable, contrasting with the bluish-grey, semi-translucent, viscid colonies of the gonococcus. The latter ferments dextrose, while catarrhalis does not.

The diagnosis of the gonococcus from the meningococcus depends on a number of small differences, and, as these can only be demonstrated by tests carried out with minute care, the task is one which should only be entrusted to a skilled pathologist with the resources of a well-equipped laboratory at his command. We do not propose to discuss these differences in any detail, but, speaking generally, the meningococcus is less sensitive to changes in temperature and reaction of medium, grows more rapidly on serum agar, and its colonies are more opaque than those of the gonococcus, while it can generally be cultivated on plain nutrient agar. Blair Martin lays stress on the fact that colonies of meningococcus grown on his medium have a very transparent outer zone with almost invisible edge, which contrasts with the well-defined wavy mar-

gin of the gonococcus colony. Meningococcus degenerates much more rapidly than gonococcus and has to be subcultured much more frequently than the latter organism to prevent its dying out altogether. Meningococcus forms acid with maltose and dextrose, while gonococcus ferments only dextrose. Serological tests have also established the close relationship which exists between the gonococcus and the meningococcus.

CHAPTER II

PATHOLOGY (*continued*)

CONDITIONS GOVERNING INFECTION

Virulence.—Under artificial conditions of growth the gonococcus gradually loses its virulence, till after the thirtieth generation it is no longer capable of infecting the most susceptible of tissues. Under other extracorporeal conditions, as when infecting such articles as towels, napkins, etc., the period of its virulence probably corresponds very closely with that of its vitality.

It is uncertain whether the gonococcus declines in virulence with long residence in one host. In old-standing cases of gonorrhœa the symptoms are generally so mild, in spite of the presence of gonococci, that either the patient has acquired a tolerance of the micro-organisms or the latter have lost the greater part of their toxic power. The latter explanation is supported by the fact that an exacerbation of symptoms is apt to

follow any circumstance, such as over-indulgence in alcohol or sexual intercourse, which is likely to cause an increased determination of blood to the part, carrying with it fresh nutritive material for the gonococci present. That the mucous membrane has not acquired a complete tolerance is shown by the fact that if a man suffering from old-standing gonorrhoea marries, even when the only evidence of his gonorrhoea is the presence of gonococci in his urethra, or its adnexa, he infects his wife and may himself develop an acute attack of gonorrhoea through infection with his own gonococci, whose virulence he has restored by passage through another host.

Some authorities hold that chronic gonorrhoea in the male causes chronic gonorrhoea in the female, indicating that the gonococcus has permanently lost some of its former virulence, but this has not been supported by further investigation, which shows that gonorrhoea in women, as it is very frequently a cervicitis, may be almost symptomless in spite of very acute inflammatory changes in the parts affected.

Susceptibility of Men and Animals.—Lower animals are infected with difficulty ; it is possible to kill guinea-pigs and mice by injecting them with sufficiently large doses of gonococci, and intra-peritoneal injection results in the production of a local infiltrate, but no conclusive results have been obtained by attempts to induce gonorrhoeal urethritis in lower animals, even in monkeys.

Human beings, on the other hand, have almost always shown themselves susceptible to experimental inoculation of some part of the genito-urinary tract. Probably the susceptibility of different individuals varies, though many of the experiences which go to show this, e.g. coitus of a number of men with one woman suffering from gonorrhoea and infection of only a certain proportion of them, are open to the objection that under these natural conditions the circumstances favourable to the implanting of the gonococcus on the urethral mucous membrane may vary (long prepuce, duration of the sexual act, subsequent washing, etc.). On the other hand, gonococci have occasionally been found in-

habiting the genital tract of a wife or husband without their presence in the partner, and it is difficult to explain this on other grounds than natural immunity of the latter.

Susceptibility of Different Human Tissues, and Paths of Infection.—Speaking generally, the mucous membrane lining the genito-urinary tract is more susceptible to infection than any other tissue of the body, and in adults transfer of the disease is almost invariably accomplished by coitus.

Probably circumstances accompanying the sexual act are specially conducive to the gonococcus reaching favourable sites for its growth. This is easy to understand in the case of the adult female in whom susceptible parts, the cervix uteri, urethra and mouths of Bartholin's glands are easily infected by gonococci in the seminal emission, which reaches them at once. In the male urethra the explanation is not so simple, however. The glans penis and fossa navicularis are very resistant to the gonococcus, which is also a non-motile organism; before gonorrhoea can result, therefore, the micro-

organisms must be carried beyond these regions to the highly susceptible cylindrical epithelium of the mucous membrane behind the fossa before they are removed by mechanical means. There is reason to suppose that the increased secretion from Littré's glands, which accompanies the sexual act, provides at once a means of adherence for the gonococcus and a favourable medium for its growth. The infecting gonococci must primarily be planted on the lips of the meatus, either directly or by the subsequent rubbing of an infected prepuce over them. The lips of the meatus being slightly everted just after coitus provide at this time a greater adhering surface than normally. Once inside the fossa navicularis the gonococcus lies in a favourable culture medium and grows fairly rapidly over the surface, its spread backwards being possibly assisted by mucous currents, though it may not penetrate between the epithelial cells at first and is exposed to risk of mechanical removal.

The success which has attended prompt measures to remove gonococcal infection by mechanical and chemical means, especially if these are

carried out within the first twenty-four hours, is evidence that in most cases the specially vulnerable cylindrical epithelium is not reached till the second day. The lesson of this, from the hygienic point of view, is that in the early hours following exposure to infection there is a golden opportunity of preventing the gonococcus from obtaining a foothold in the male urethra.

Under other circumstances, mere contact of the gonococcus with the penis is not often followed by infection, since it has been found that in epidemics of vulvo-vaginitis in children's institutions, boys exposed to the same chances of infection do not develop gonorrhoea.

Any other means by which the gonococcus can be carried to susceptible parts, such as infected instruments, can, of course, cause gonorrhoea.

In little girls, in contrast to adult females, it is the inner surface of the vulva and the vagina which are most susceptible, and it is easy to understand, remembering this and the prominence of the external genitals in these subjects, how easy it is for the gonococcus to obtain a

foothold without gross penetration of the genital tract.

Regarding other parts to which the gonococcus can spread after its introduction and the onset of gonorrhoea, the ducts of all glands which open on to the mucous membrane of the male urethra, are as susceptible to infection as the mucous membrane itself.

Exactly how the infection reaches the posterior urethra is uncertain. It is generally believed that a barrier to its spread exists at the anterior opening of the triangular ligament; possibly, as Scholtz believes, the compressor urethrae tends to prevent the regurgitation of pus, or, as Finger holds, the membranous urethra, having no glands opening on to it, gives the gonococcus no cover. In any case, we have reason to believe that this obstacle is overcome sooner or later in the majority of cases without any assistance from outside, in the form of instruments, irrigation, etc., and it is possible that the infection is carried along the wall by mucous currents in some cases, while in others, the pus, unable to obtain an exit quickly enough

through the meatus, is squeezed back through the membranous urethra.

How often the vas deferens is infected by the introduction of gonococci into it cannot be determined, but a number of cases are now on record in which it was found that the vas was healthy though the epididymis was infected. On this account some authorities believe that gonorrhoeal epididymitis is very often due to gonococci conveyed by the blood or lymph stream, but the evidence is in favour of the vas being the route of infection. Oppenheimer and Low, Schindler and others have shown that when the caput gallinaginis is inflamed and is irritated by chemical or mechanical means a reverse contraction of the involuntary muscle fibres of the vas occurs, and this would carry infecting material back towards the epididymis. Infection of the vas often occurs, however, and the same applies to a greater extent to the vesiculae seminales.

The mucous membrane of the bladder must often be brought into contact with gonococci, but severe gonorrhoeal cystitis is not

common. Whether this is due to greater resistance of the bladder mucous membrane, or to the bactericidal action of the urine, or its diluting effect on the toxin of the gonococcus is an open question. The pelvis of the kidney may be infected by gonococci carried back through antiperistaltic action of the ureter, but pure gonococcal infections of the kidney pelvis are not common, most of the severe cases of pyelitis occurring in the course of attacks of gonorrhoea having been due to other bacteria.

In the female adult the lining membrane of the uterus and that of the Fallopian tubes are very susceptible, while the ovaries have been found infected in certain cases. By extension, either through the ostium abdominale, or directly through the wall of the Fallopian tube, gonococci can gain access to the peritoneum, but the latter structure usually shows by its ability to limit the infection to a comparatively small area that it is very resistant. Whether the gonococcus always succeeds in infecting the upper genital tract in women whenever it gains access to it cannot be determined. Disease

of these parts is more common in gonorrhoea of women after the birth of the first child, but this may be due to special circumstances having enabled the gonococcus to obtain a better foothold, rather than to any increased susceptibility of the patient. At the time of the puerperium the uterine cavity contains a much larger amount of blood serum, in which gonococci would grow freely and rapidly spread over the surface towards the tubes ; possibly, too, the process of childbirth removes a mechanical barrier which previously existed.

The rectal mucous membrane is very susceptible in both sexes. It has been found diseased most often in women, but this is probably due to the greater chance of the gonococci being conveyed to it directly from the genital tract, rather than to any lower resistance.

Of parts to which the gonococcus can be transferred by other means than sexual intercourse, or the circulation, by far the most important is the conjunctiva. The conjunctiva of new-born infants is much more frequently infected than that of adults. Probably the greater mass of gono-

cocci conveyed to it during its passage through the infected genital tract of the mother, coupled with the smaller protecting reflex activity of these parts in infants, are responsible for this, as well as their greater susceptibility. The mouth is only susceptible to the gonococcus in new-born and very young children, while the nose and ears are practically never infected.

No tissue which the gonococcus can reach through the lymphatics or blood-vessels is completely resistant to infection, though the susceptibility of these parts is much less than that of the genital mucous membrane or the conjunctiva. Probably the gonococcus gains entrance to the circulation in gonorrhoea and gonorrhoeal ophthalmia much more frequently than metastatic complications occur, as is shown by the facts that gonococci have been recovered from the blood stream in cases of uncomplicated gonorrhoea and that in some cases the *locus minoris resistentiae* provided by a local injury has determined the formation of a gonococcal abscess; so that the occurrence of metastases points rather to personal susceptibility of the

patient than to special severity of the mucous membrane lesions, or anatomical peculiarities, facilitating the entry of gonococci into the circulation.

Of all the tissues which the gonococcus can reach by means of the circulation, the synovial membrane of joints is by far the most frequently infected, while next in point of frequency come the iris and the endocardium. On comparatively rare occasions gonococci have been found infecting the pleura, pericardium, myocardium, subcutaneous and perinephric tissues, periosteum and even the central nervous system, as well as lymphatics and inguinal glands and veins of the penis and legs.

PATHOLOGICAL CHANGES PRODUCED BY THE GONOCOCCUS.—As we have already stated, the gonococcus is, above all, a parasite of certain mucous membranes, especially those of the genito-urinary tract, the eye and rectum, and it is in the portions of these which are lined with cylindrical epithelium that its most profound effects are produced. Having gained a foothold on such a mucous membrane it begins to spread over

the surface, and follows the latter down the ducts of all glands which open on it, but no visible effects of its growth are apparent for a period varying from two to thirty (generally three) days. At the end of this, the incubation, period its toxin, which is probably set free by disintegration of dead and degenerated cocci, has accumulated in sufficient amount to damage and irritate the mucous membrane and severe hyperaemia occurs, with exudation of serum.

This corresponds to the commencement of clinical signs. The epithelial cells become swollen and separated from one another by the serous exudate passing from the vessels below to the surface, and the gonococci commence to grow down between them towards the subepithelial connective tissues, which they eventually reach. The epithelial cells, becoming degenerated and loosened, are cast off in large numbers, constituting a large proportion of the discharge at this stage of the disease. The shedding of epithelium may be so extensive in places that the subepithelial connective tissue is laid bare, leaving eroded patches. The serous exu-

date is rapidly followed by one containing cells from the vessels in the subepithelial connective tissue, the exuded cells consisting for the most part of polynuclear leucocytes, with a considerably smaller number of lymphocytes, which pass through the epithelium and appear in the thick creamy discharge characteristic of this stage of the disease. Sometimes numbers of red blood cells are exuded when the affected part is particularly vascular, as in the posterior urethra and the uterus.

Coincident with this, the connective tissue, with the longitudinal and circular muscle fibres, underlying the epithelium, becomes infiltrated with round and plasma cells, the infiltration being always most marked in the superficial layers, where also the gonococci are to be found in greatest numbers. The extent of the infiltration varies, in some cases being limited to the superficial layers of the subepithelial connective tissue and in others involving the tissues much more deeply. In the penis the trabeculae of the corpus spongiosum may be more or less densely infiltrated, and the interference with the entry of

blood into the erectile tissue consequent on this, together with spasm of the longitudinal muscle fibres underlying the mucous membrane, is responsible for the chordee, which frequently occurs in the acute stages of gonorrhoea.

Though large numbers of round cells are scattered throughout the connective tissue they are especially densely aggregated round the mouths and ducts of glands which open on the mucous surface, and here also the epithelial cells are more severely damaged than on the surface. Polynuclear leucocytes, many containing gonococci, are seen amongst the round cells, especially in the superficial layers.

The mucous membrane becomes swollen in consequence of the above changes and loses its elasticity, so that it cannot conform to alterations in the size of the surrounding erectile tissue, and erections are extremely painful. The connective tissue vessels are distended with blood containing large numbers of leucocytes and may become thrombosed in places, while lymphangitis and perilymphangitis may sometimes occur.

Gonococci are found on the surface almost

entirely enclosed within polynuclear white cells; between the epithelial cells they are aggregated into small heaps in some places, while in others they form single rows which follow the contour of the cells so as apparently to enclose the latter in a network, but they do not penetrate the epithelial cells. In the subepithelial connective tissue they occur extracellularly, as well as enclosed within polynuclear cells; as above mentioned, they are found most numerously in the superficial layers.

Mucous membranes which are lined with squamous epithelium, such as the fossa navicularis, the vagina, and mouth, do not show such severe changes as those lined with cylindrical. Gonococci may penetrate between the epithelial cells but do not often reach the deeper layers of these, nor the subepithelial connective tissue. The latter is not so densely infiltrated as that which underlies cylindrical epithelium.

Owing to the inflammatory changes in and round the mouths and ducts of glands opening on the mucous membrane, they frequently

become blocked, and the gland cavity then becomes filled with inflammatory exudate, epithelial cells and gonococci, forming a pseudo-abscess, as Jadassohn described it. This is particularly apt to occur in the prostate, Littré's, Bartholin's and the utricular glands, as well as the two follicles which open on or near the mouth of the female urethra.

This penetration of gland ducts by the gonococcus is important from many points of view. In the case of Littré's glands the periglandular infiltration may involve the corpus spongiosum in which the gland is imbedded and is then quite probably an important cause of the infiltration of that structure in gonorrhoea. In the prostate, dense infiltrations are imbedded in the tissue, especially round the vessels and glands, and the extensive involvement of this organ which frequently occurs is due to the fact that the glands imbedded in it afford the gonococcus a means of approaching its deeper parts. Apart from the pseudo-abscesses caused by the blocking of glands, the perivascular infiltrates in the prostate may soften in the centre

and break down into abscesses. The pseudo-abscess may become infected with other organisms, staphylococci, streptococci, B. coli, or, in the case of Bartholin's glands, B. caducus and other anaerobes, and the result depends on the infecting organism. If the latter be pyogenic the wall of the gland may be more severely attacked and, giving way, allow the contents to escape into the surrounding tissues; here they form a true abscess, which may break externally and lead to fistula.

Probably more important than the above, however, is the fact that within the gland ducts the gonococci are protected from attack or removal by chemical or mechanical means, and it is this which is responsible for much of the intractability of gonorrhoea. Long after the general mucous membrane has returned to a normal state these pockets of pus may remain. Every now and again their contents may be expressed on to the surface of the mucous membrane, where they may cause a mild exacerbation of symptoms, and, in any case, are a source of infection to others.

To what extent the above changes occur in average cases of gonorrhoea is quite uncertain, since examinations have, for the most part, been conducted in cases where ante-mortem circumstances were conducive to severe attacks; naturally, it is not easy to obtain material for post-mortem examination in acute gonorrhoea.

When the attack goes on to complete recovery the intensity of the inflammation lessens after a few weeks, the discharge becomes less crowded with pus cells, and flattened epithelium grows over the places formerly clothed with cylindrical cells. Gonococci still continue to be discharged, and the catarrhal process continues in a mild way during the restoration of the epithelial covering, but in steadily diminishing severity. Gonococci disappear from the subepithelial connective tissue, the collections of round cells are gradually removed and, finally, the surface epithelium again returns to its normal cylindrical shape.

In a large proportion of cases of gonorrhoea, unfortunately, recovery is not complete. The glands opening on to the mucous surface frequently remain diseased, or the process continues in such

parts as the seminal vesicles, to which it has spread during the acute stages, and patches of the surface mucous membrane and underlying tissue may remain chronically inflamed. In the bulbous portion of the male urethra the inflammation is especially apt to become chronic, but any part of the urethra may be similarly affected. The changes which occur in these places vary in severity. Occasionally the epithelium may be entirely absent, exposing a patch of granulation tissue. More frequently the epithelium is thickened, and its surface layers composed of flattened cells. Owing to its thickening and the local increase of granulation tissue under it the mucous membrane may project into the lumen as minute excrescences or small polypi. The epithelium may take on the characters of epidermis, or be composed throughout of many layers of flattened epithelium. The latter condition is generally found in advanced stages, when the subepithelial tissue has become converted into cicatricial tissue. The superficial layers of epithelium are constantly being shed, occasionally in large flakes.

In the connective tissue underlying these chronically inflamed areas changes occur which frequently lead to most important consequences, especially when they affect the anterior urethra. In the mildest cases, and probably when the gonococcus has not acted for long on the tissues of the urethra, only the superficial layers are infiltrated with round cells. In others, especially where many exacerbations of the disease occur from any cause, the infiltration gradually increases in density and depth opposite the diseased area till eventually it involves the whole thickness of the corpus spongiosum. Between this and the mildest degree of infiltration varying depths of the connective tissue may be involved. The infiltrating cells are gradually replaced by new-formed connective tissue cells and new vessels, and the granulation tissue thus formed is eventually converted into cicatricial tissue. The process is generally a slow one, taking years to reach its final stage. The superficial area involved in the above changes varies also from a very small and unimportant portion to the whole circumference of the canal.

The distensibility of the anterior urethra is affected according to the area, depth and age of these subepithelial changes. It is naturally most affected by those which run circumferentially and extend most deeply. In the latter, as the new-formed connective tissue is laid down and eventually contracts, the urethra is locally narrowed, and it becomes increasingly difficult to restore its calibre by means of instruments till in the worst cases only the smallest bougies can be passed.

The glands show exactly analogous changes. Sometimes the duct of the gland is widened by the contraction of surrounding tissue, but at others, it is closed and the gland converted to a small cyst with densely infiltrated walls. Eventually in these cases the contents may be absorbed, and the gland replaced by fibrous tissue.

Regarding special structures, the changes which occur in the male urethra have been sufficiently discussed in the above description. In the vesiculæ seminales the effect of gonococcal infection is much the same as when the urethral

mucous membrane is attacked, epithelium being invaded and shed extensively, while the surrounding connective tissue is often markedly infiltrated with round cells which may eventually be replaced by cicatricial tissue. The cavity contains a collection of pus and epithelial cells, but in the sections which have so far been made no spermatozoa have been found.

In the epididymis the process generally seems to be most intense at the cauda. In places the epithelium is shed entirely, in others, only its cilia-like processes are lost. As the inflammation proceeds the round-celled infiltration of the surrounding connective tissue increases, and this, with the swelling of the lining membrane, combines to block the tube, which becomes a pus-containing cavity. Complete resolution of this is exceptional; generally the round-celled infiltration round the tube becomes converted into one or more nodules of firm fibrous tissue. The blockage may be permanent, and if this occurs on both sides sterility results.

The pathological changes which follow infec-

tion of the female genital tract are essentially the same as those which occur in the male, differing only in the after-effects, which depend on the anatomical relations and physiological functions of its different parts. The urethra, not having so many glands opening into it, and being shorter, develops an inflammation the effects of which are not so far-reaching as in the case of the male urethra. Two follicles which open on either side, one at or just within, the other close to the opening of the urethra, often become infected and filled with pus, which may be discharged intermittently. They are mentioned because they are sources of infection which may pass unnoticed.

The vagina being lined with squamous epithelium, the changes produced by the gonococcus in it are not nearly so profound as in mucous membrane covered with cylindrical epithelium. As already stated, it is chiefly in young children that the vagina is affected. In these the mucous membrane becomes hyperaemic and its papillae swollen and infiltrated so that these may protrude as small polypi, especially in the posterior wall

and where the mucous membrane of the vagina joins that lining the uterus at the external os. In places, chiefly on the apices of the papillae, the epithelium degenerates and is shed so that it may be reduced to a few layers of cells, or the subepithelial connective tissue laid bare. Gonococci are found in clumps between the epithelial cells and may penetrate as far as the subepithelial connective tissue, particularly where all the epithelium has been removed.

Gonococcal infection of the vulva is an affection which is practically confined to young children. In adults inflammation of the vulva may result from irritation with gonorrhoeal discharges, but inflammation primarily due to gonococcal infection is rare. In children it may arise as a result of infection by fingers of adults, by infected towels, napkins or bath-water, or in the new-born as the result of passage through the infected genital tract of the mother. The mucous membrane becomes hyperaemic and oedematous, there is marked exudation of leucocytes, and the epithelium may be completely shed in places, leaving eroded patches

or fissured ulcers. The follicles are similarly affected, as well as the ducts of Bartholin's glands, and the infection often spreads to the urethra and vagina. After the inflammation of the surface mucous membrane has healed the follicles lining the inside of the labia minora and those which open in or near the mouth of the urethra may remain diseased.

Bartholin's glands are frequently infected in the gonorrhoea of females, whether this commences as a urethritis, vulvo-vaginitis, or cervicitis, and the process is much the same as occurs in other gonococcal infections of glands which open on to mucous membrane. Most authorities agree that it is the tissues of the gland ducts which are chiefly invaded. The epithelium of these is shed entirely in places, becoming replaced by flat epithelium, and the periglandular connective tissue infiltrated with round cells, which may be densely aggregated round the mouth of the gland. As a result of the swelling and surrounding infiltration the duct of the gland may become blocked and its cavity converted to a pseudo-abscess containing degenerated epithe-

lium, pus cells and gonococci. The contents may become infected with other organisms, anaerobes such as B. foetidus or B. caducus, which make them foul smelling, or staphylococci or streptococci, which set up a more acute inflammation, cause softening and giving way of the wall and the formation of a true abscess in the surrounding tissues. This may break through the skin between the two labia, or find its way to the perineum or into the rectum. Bartholin's glands are amongst the most frequent lurking places of the gonococcus in chronic gonorrhoea of women, and intermittent discharge of their contents on to the surface of the mucous membrane makes them a regular source of infection to others.

The cervix uteri is one of the most frequent sites of gonorrhoea in women, being often the first place to be infected, and is the starting-place for infection of the higher genital tract. In acute gonorrhoea the pathological changes which occur here and in the lining membrane of the uterus are similar to those following infection of other mucous membranes which are lined with cylindrical epithelium.

The whole surface of the mucous membrane may be affected, or the process confined to the mouths and ducts of the glands, especially in the cervix. The cylindrical epithelium is extensively shed and replaced at first by flat cells. The hyperaemia may be so intense that the exudation contains many red blood corpuscles. Gonococci are found on the surface, between the epithelial cells and in the deeper layers of the mucous membrane, while they have also been found in the vessels of the cervix, as well as imbedded in the muscle. The whole uterus is often infiltrated with round and polynuclear cells and its vessels are distended with blood.

In cases which become chronic, or are so from the first, the mucous membrane is either generally swollen, with hypertrophied papillae which sometimes become polypoid, or atrophied and covered with flat epithelium, the surface layers of which are keratinized. As in other mucous membranes, the numerous glands, especially those lining the cervical canal, are generally affected, and their mouths frequently become

blocked either temporarily or permanently, in the latter case being converted to cysts. This is a frequent cause of Ovula Nabothi in the cervix. The process is often confined to a few isolated spots, where the epithelium is flattened and possibly its superficial layers keratinized, while the rest of the mucous membrane remains covered with cylindrical epithelium. From time to time the inflammation may become acute again, and this is specially apt to occur at childbirth and in the puerperium, so that what was at first a purely local affection, confined to the cervix and perhaps a few small areas in the uterus, may spread widely upwards and infect the tubes, ovaries and peritoneum covering them.

Infection of the Fallopian tubes naturally derives its importance from the anatomical relations and physiological functions of these structures. In the mildest cases the epithelium loses its cilia, or is entirely shed and replaced by flattened epithelium. If the process remains at this stage, and with the tube patent, spermatozoa can move along it to the ovary, but the ova when impregnated cannot be carried

into the uterus, and most observers lay stress on this as a cause of tubal pregnancy. In more severe infections the walls of the tube are extensively infiltrated, and gonococci penetrate deeply into them. The tube becoming blocked is converted into a cavity containing pus and other inflammatory products. The gonococci can penetrate through the wall of the tube, and a local inflammation of the peritoneum results.

Included in this is the peritoneal covering of the ovary, from which the infection may spread inwards, setting up inflammatory changes within the organ. Infection may also be carried to the ovary through the circulation via the hilus. The pus from the Fallopian tube may burst through the ostium abdominale and similarly cause local inflammatory changes in the peritoneum.

In whatever way the peritoneum becomes infected the result is usually the formation of considerable fibrous tissue in the pelvis, and consequent interference with the functions of the uterus, ovaries, and pelvic viscera. The gonococci in a pyo- or hydro-salpynx seem eventually

to die out in most cases, and the collection may remain sterile, but sometimes this becomes infected with other organisms, and, instead of a purely local peritonitis resulting from the entry of the tube contents into the peritoneal cavity, general inflammation is more likely to follow.

In gonorrhoeal ophthalmia due to gonococci introduced from without, owing to the penetration of gonococci between them the epithelial cells are extensively shed; the subepithelial tissues are engorged with blood and infiltrated with leucocytes, which also pour through the epithelial layers and appear in the profuse purulent discharge. The cornea may slough owing to interference with its nutritive supply as well as to extension of infection to it, and the whole eye become involved in the acute inflammatory changes.

As we have already stated, the most constant manifestation of gonococcal septicaemia is infection of the joints and periarticular tissues. In gonorrhoeal synovitis the endothelium is rapidly shed, and the joint becomes filled with a sero-purulent exudate containing many pus cells

and gonococci, the latter being both free and contained within the pus cells. The synovial membrane becomes swollen and covered with granulations, the cartilage may be eroded, and the periosteum of the neighbouring bones inflamed.

Microscopically, Finger found in two such cases the inner layer of the synovial membrane covered with pus cells, either free or enclosed in a fibrin-like network, and containing numerous gonococci; next to this was a homogeneous or slightly granular layer containing few intact pus cells, many free nuclei and some gonococci, while between this and the periarticular tissue was a broad layer of granulation tissue consisting of mononuclear spindle and polygonal cells surrounding numerous capillaries, as well as scanty pus cells, some of which contained gonococci. The cartilage was infiltrated and contained a small cavity filled with pus cells, and between the cartilage and the perichondrium was a collection of pus cells.

The bursae which communicate with the joint frequently become similarly infected by direct extension. Gonococci tend to disappear

quickly from the joint cavity, probably because the character of the fluid changes and becomes unfavourable to their growth. The fluid exudation into the joint is sometimes excessive, and hydrarthrosis results.

The inflammation may subside completely, or the granulation tissue go on to formation of cicatricial tissue, which, with the periosteal and perichondrial changes and those in the cartilage itself, may lead to more or less complete anchylosis. If other organisms gain access to the joint through the circulation during the acute stage, acute septic arthritis may result.

Instead of the synovial membrane, the chief site of the gonococcal infection may be in the periarticular tissues, which become intensely infiltrated with round cells. The process may resolve completely, or the round-celled infiltration be replaced by cicatricial tissue leaving the affected ligaments considerably weakened. An important site of infection is the tarsus, and flat-foot is a common result of the weakening of the supporting ligaments which occurs.

Gonococci may infect the periosteum, especi-

ally of bones which enter into the formation of affected joints ; apart from the latter, the tibia, scapula, clavicle, manubrium sterni, and the os calcis at the insertions of the tendo Achillis and the plantar ligament have been found affected. The process, which consists in a local round-celled infiltration under the periosteum, does not frequently result in pus formation. Similarly tendon sheaths, muscles and fasciæ may occasionally be infected, especially those in connexion with affected joints, but these require no special description. The process is essentially the same as in the joints, and there is the same tendency of the round-celled infiltration to result in cicatricial tissue formation, which limits the function of the affected part.

In the heart gonococcal invasion produces more or less severe ulcerative endocarditis, and the process may spread to the myocardium and pericardium. In a case described by Finger, Ghon and Schlägenhaufer, the vegetations, which were chiefly situated on or near the valves, were built up of a framework of blood plates held together by threads

and strands of fibrin. In the central clefts and spaces enclosed by this framework were broken-down cells and gonococci, while those in the periphery contained numerous leucocytes, many containing gonococci, as in gonorrhoeal pus. Some of the spaces were filled with colonies of gonococci arranged as in cultures, the organisms in the centre being involuted and only those at the periphery normal in size and shape. In other places clefts were filled with gonococci arranged in single line formation. The right aortic valve was perforated, and under it the myocardium was destroyed to the extent of a centimetre broad and some millimetres deep. As in similar conditions due to other pathogenic micro-organisms, infarcts are common in the viscera, but, unlike them, do not seem to form fresh foci of inflammation.

In gonorrhoeal iritis the ciliary vessels are congested, and there is exudation of serum and round cells into the tissues of the iris. The surface of the latter is covered with this inflammatory exudate which is also poured into the anterior chamber, sometimes causing hypopyon.

The iris becomes more or less extensively adherent to the lens. In the early stages the adhesion is by means of serum and exuded cells and can easily be broken, but where resolution is not complete the cells become replaced by new connective tissue and the adhesions firmly established. The pathological pictures of pleurisy, pericarditis, subcutaneous abscesses and thrombo-phlebitis, which occasionally complicate gonorrhoea, require no special description, their essential characteristic being the presence of the gonococcus.

Certain complications of gonorrhoea have been ascribed to the effect of gonotoxin, chiefly because of failure to find the gonococcus in the affected parts. Amongst these may be mentioned a milder form of conjunctivitis than the purulent ophthalmia which follows direct infection from without, retinitis, optic neuritis, various disturbances of the nervous system, peripheral or central, and various skin affections, such as urticaria, erythemata, purpura and the interesting condition known as "hyperkeratosis blenorrhagica." That in spite of failure to find

gonococci locally in these lesions they depend in some way on gonococcal infection is sufficiently shown by the way they disappear with the recovery of the patient from the gonococcal attack and reappear with each recrudescence of the latter. Some cases of gonorrhoeal rheumatism have been attributed to toxin only, but probably the failure to find gonococci in the joint fluid of these cases was due to the puncture having been delayed till they had disappeared.

Hyperkeratosis is a rare affection which chiefly affects the skin of the soles and the dorsum of the toes, as well as the palms of the hands. It consists of an infiltration of the papillae and Malpighian layer with leucocytes, which are also exuded into the epidermis. The affected papillae become swollen, the cells of the Malpighian layer more or less separated from one another by the leucocyte infiltration, and the stratum granulosum is replaced by numerous layers of partly keratinized flat cells of which the nuclei have disappeared; between these, fragments of broken-down leucocytes may still be

found. The process may be confined to a few small scattered areas, or the whole sole may be affected.

HISTOLOGY OF GONORRHOEAL PUS.—Much has been written on the microscopical examination of gonorrhoeal pus in the various stages of the disease, and many workers have from time to time attached considerable importance to its cytology from a diagnostic and prognostic point of view, but their conclusions have varied so much, often directly contradicting one another, that we must confine ourselves to general remarks on the subject. In the early stage, when the discharge is mucous in character, it consists for the most part of epithelial cells, plentifully sprinkled with gonococci, which also occur in heaps between the cells. After a few days, when the discharge becomes thick and creamy, it consists almost entirely of polynuclear leucocytes, some lymphocytes, plasma cells, mast cells, and very scanty epithelium. In a properly spread film the gonococci will be found almost exclusively contained within the polynuclear cells; some of these may be liter-

ally stuffed with cocci, while others contain twenty or thirty or perhaps only a few pairs, and the majority none.

The presence of coarse-grained eosinophile cells, in much larger proportions than they occur in the blood generally, has attracted considerable attention. They appear to become more frequent from the third or fourth week, but their significance is by no means decided.

With the decline of the acute stage the polynuclear leucocytes diminish in numbers, and epithelial cells begin to occur more frequently till in the thin watery discharge of the last stages and of very chronic cases epithelial cells may even preponderate. In the later stages it may be hard to find gonococci within the pus cells as they are then chiefly extracellular.

The threads frequently found floating in the urine of gonorrhoea cases consist of pus cells containing gonococci, epithelial cells and mononuclear leucocytes for the most part. They are important because gonococci can often

be found by examining them when search in other directions has failed.

THE BIOLOGICAL RELATIONS OF GONOCOCCI TO THE TISSUES.—Speaking generally, gonococcal infections seem to commence as acute processes and to end as chronic, and it appears as if the tissues made a great effort at first to remove the infecting organisms, but eventually came to tolerate their presence under mild protest. In this respect, they differ from the majority of streptococcal and staphylococcal infections, in which invading micro-organisms and tissues wage a fiercer battle, with a more decisive issue. Exactly by what process the body defends itself against the gonococcus, and finally removes it, is uncertain. In the acute stages of gonorrhoea the polynuclear leucocytes in the discharge contain almost all the gonococci to be found in it; on this account many workers believe that the gonococcus is a parasite of polynuclear cells, in which it also multiplies, and that its extra-cellular life is a short one. There are many very strong reasons against this belief, some of which we may shortly mention.

Gonococci are non-motile and would fare poorly if they depended on some benevolent leucocyte to move towards them so that they could penetrate it. Polynuclear cells containing gonococci show no signs of any damage having been inflicted by the latter; on the contrary, if gonococcal pus be stained with neutral red, the intracellular cocci are dyed red, while the extracellular ones remain unstained. The staining of ingested organisms by means of neutral red was used by Metchnikoff to demonstrate the secretion of an acid peptic fluid by the phagocyte, and the neutral red staining of intracellular gonococci would indicate a similar action on the part of gonorrhoeal pus cells. Between the epithelial cells gonococci are almost entirely extracellular, while in the submucous connective tissues more of them are extra- than intra- cellular, so that evidently gonoccoci do not depend for their existence on nourishment derived from the protoplasm of a polynuclear leucocyte. Also, if dead gonococci and polynuclear cells be placed in contact, the former will very soon be found included within the latter.

There is much more reason, therefore, for believing that the presence of gonococci within the pus cells simply indicates that, in conformity with its usual habit in the presence of a bacterial infection, the body institutes a counter-attack by means of its polynuclear leucocytes, which, again in conformity with their nature, enclose the invading organisms. The fact that the latter are more easily phagocyted than most other pathogenic organisms merely indicates that they are less poisonous. That the gonococci are apparently little damaged by the process of ingestion indicates to us simply that they are passively resistant to such attack as the phagocyte can direct against them, just as, for example, would be particles of carbon. The phagocytosis occurs chiefly on the surface of the mucous membrane, since if all the discharge be washed away from the surface and more be expressed from the deeper layers and examined at once the gonococci in it will be found to be chiefly extracellular.

It is generally believed that, in any case, phagocytosis plays only a very small part in removing

gonococci from mucous membranes, as in spite of the extensive ingestion of the micro-organisms by leucocytes, which is apparent in the discharge, the gonorrhoea continues acutely for weeks. It must be remembered, however, that by the time they have called forth an exudate of leucocytes the gonococci have already penetrated between the epithelial cells, and it seems to us very probable that here they are mechanically protected against capture by the phagocytes, which cannot move freely between the cells, so that, in spite of the enormous numbers of gonococci taken up on the surface, there remain others below it to carry on the process.

Our own belief is that phagocytosis plays a more useful part than is generally supposed. In other words, that if phagocytosis did not occur the disease would be a much more extensive and severe one than it usually is. This does not mean that if numbers of extracellular cocci are found in the ordinary discharge of the acute stages the prognosis is bad, as some have thought, because it is always possible to prepare a specimen of

gonorrhoeal pus showing numerous extracellular cocci by spreading it roughly. Some slight support for the belief that phagocytosis plays a useful part in the defence is afforded by some unpublished work which Lieut. C. H. Harold, R.A.M.C., carried out at the Military Hospital, Rochester Row. He administered hetol intravenously in increasing doses to a series of cases of subacute gonorrhoea a few days after giving gonococcal vaccine to them, hoping to increase the number of exuded leucocytes and thereby cause an even more extensive phagocytosis than usually occurs. The result in each case was a marked increase in the discharge some hours later, but in every one of the cases treated in this way the gonorrhoea ran a shorter course.

The part which antibodies in the blood-serum play in gonococcal infections of mucous membranes is undecided. It is fairly widely stated that they cannot be demonstrated in gonorrhoea, that their artificial increase by means of vaccines does not affect the course of the disease and that, therefore, they are unimportant here.

Certainly, judging by the complement deviation test, their presence is not so marked as in gonorrhoeal arthritis, though we have, on occasion, demonstrated them by this test in acute posterior urethritis. On the other hand, Eyre and Stewart found in acute gonorrhoea, and Hamilton and Cook in vulvo-vaginitis, that when the opsonic index was steadily above normal the progress was better than when it was fluctuating widely, or persistently below normal; so that, if we may rely on the opsonic index as a guide to the amount of antibody in the blood, the above statement requires revision. Further, we are convinced that artificial increase of antibodies by means of vaccines has a beneficial effect in gonorrhoea. Certainly the purulent discharge may persist for as long, but the milder course which our cases have pursued under vaccine treatment, as well as the good results claimed by Eyre and Stewart in uncomplicated gonorrhoeal urethritis, is evidence that if the antibodies be increased with vaccines they prevent the gonococcus from penetrating so deeply as they otherwise would. We think that antibodies

and phagocytes work hand in hand in this respect; they may not be able to exterminate the gonococcus finally without the help of other processes, but it seems to be as much a mistake to look to one process only to explain the cure, as to rely exclusively on one branch of an army for its victory over an enemy.

Scholtz, Bumm, Jadassohn and others hold that it is the change in the character of the epithelium in gonorrhoea which is chiefly responsible for the final removal of gonococci from mucous membranes. Flat-celled epithelium, with which the cylindrical epithelium is at first replaced in gonorrhoea, is always more resistant to the action of gonococci. These may penetrate between the flat cells and occupy spaces there, but do not reach the subepithelial tissues, which are left to deal with those cocci which invaded it in the earlier stages. In addition to this, the cylindrical cells, with which the flat-celled epithelium is finally replaced, seem to enjoy a considerable degree of immunity to the gonococci *in situ*, though possibly not to others introduced from without.

In the subepithelial connective tissue the round-celled infiltration, which always tends to the production of cicatricial tissue, acts as a barrier not only to the further penetration of gonococci into the tissues but to the arrival of nutritive material from the blood stream.

It seems reasonable to suppose, therefore, that the tissues, unable to exterminate the gonococci completely by such customary processes as phagocytosis and the production of antibodies when it is growing on its optimum medium, cylindrical epithelium, defend themselves by converting that medium to a less favourable one, and such gonococci as have survived mechanical removal, the influence of antibodies and phagocytosis gradually die out.

When the gonococcus trespasses beyond the limits of the mucous membrane, as in the various metastases, it is, speaking generally, on a less favourable soil and more amenable to attack by antibodies and phagocytosis. The presence of antibodies in the blood serum of patients suffering from these complications has been demonstrated by Bruck and others by means of the

complement deviation test, and their artificial production by inoculation of gonococci into animals has been shown by Torrey, Wollstein and others by the same means. The brilliant results which frequently follow the injection of vaccine, and the good effect claimed by Torrey and others for his antigonococcal serum (in which we have demonstrated considerable amounts of antibody by the complement deviation test) in the treatment of gonorrhoeal arthritis and other gonococcal metastases, indicate that immune bodies play a very considerable part in bringing the disease to an end as far as metastases are concerned.

On the other hand, neither gonorrhoea nor any of its complications leaves the body immune to attack. Future attacks of gonorrhoea may be less severe but, if anything, a patient who has suffered from a complication seems to be more prone to the same complication with each fresh attack of gonorrhoea.

THE LABORATORY DIAGNOSIS OF GONOCOCCAL INFECTIONS.—In the acute stages of gonorrhoea in the male there is no difficulty in establishing

the diagnosis by means of the microscope. Care should be taken to obtain the discharge from the urethra, as a case of balanitis with a long prepuce shows a very profuse discharge which simulates that of gonorrhoea very closely. To obtain an even film the drop of pus should not be rubbed about on the slide with a platinum loop, but spread like a blood film. In old-standing cases of gonorrhoea when the discharge is scanty, and possibly intermittent, the diagnosis may be a matter of considerable difficulty. It is just in these cases, however, that laboratory methods are most required, since it is clinically impossible to determine whether the patient is still suffering from gonorrhoea or only from the catarrh which frequently follows it after gonococci have disappeared from the urethra.

Numerous methods have been devised with the object of bringing any gonococci which may be lurking in or about the urethra to the meatus, for transfer to a microscope slide or culture medium, and of these the following may be mentioned :—Irritation of the urethra by means of chemicals, such as the injection of 1 in 20,000

perchloride of mercury or ½ to 1 per cent. silver nitrate; irritation by passage of bougies or dilators, combined possibly with massage of the urethra over the instrument; indirect irritation by administering beer or spices to the patient, or by means of sexual intercourse, with the use of a condom; massage of the urethra, prostate, seminal vesicles and Cowper's glands; injection of 3 to 6 per cent. perhydrol, with the object of carrying the gonococci to the meatus mechanically. Of these, the irritant measures and, to a certain extent, massage act by producing a greater flow of blood to the part, carrying with it more nutritive material for the gonococci, which multiply and are then more easily detected. Ballenger recommends that in addition to irritation the meatus should be sealed for several hours afterwards so that the gonococci may have a chance of multiplying before they are washed away. Needless to say, antiseptics should not be used as the irritating agents if we desire to cultivate the organisms.

We have found the following plan, which is largely based on Pick's recommendations, most

useful in dealing with chronic cases. If any discharge can be obtained from the urethra in the ordinary way it is stained and examined. The patient is then made to urinate into four glasses without stopping the flow at any time, and the urine searched for threads. If it is turbid from phosphates it is first cleared with acetic acid. Any threads which are found are fished out and spread on a microscope slide. The following method of doing this is very successful:—The thread having been transferred to the slide, as much as possible of the fluid which accompanies it is removed with blotting paper; the slide is then left in a sloping position to allow one end, the upper, to dry and fix the thread to the slide; it is then spread out evenly by means of another slide and stained. Failing the finding of gonococci in threads, the urine is centrifugalized, the deposit suspended in physiological salt solution and again centrifugalized. Whether gonococci are found or not, the urethra is then washed with salt solution till the latter returns quite clear, and a little sterile salt solution is injected into the bladder. The prostate

and seminal vesicles are then massaged, and any discharge which appears at the mouth of the meatus as a result of this is examined for gonococci. The patient passes the salt solution which has been injected into his bladder, and this is examined for gonococci in the same way as when dealing with urine. Should these be found one can infer that the prostatic glands or seminal vesicles, or both, are infected. At a subsequent sitting Cowper's glands are similarly massaged after washing out the urethra. The anterior urethra is examined in the following manner. The urethra having been washed clean in the usual way, the glans penis is grasped between the finger and thumb of the left hand, and the penis put on the stretch ; then, with the thumb of the right hand on the dorsum and the index and middle fingers pressing against the urethra below, the latter is massaged from the bulb towards the meatus. The anterior urethra is then washed out with cold saline, so as to induce a spasm of the compressor urethrae and prevent any of the fluid passing into the posterior urethra, and the wash water examined for gonococci.

In some cases a bougie, or a Kollmann's dilator is passed, and the urethra massaged over it.

This method of examination not only affords information as to the localities in which the gonococcus is lurking, but, incidentally, reveals any abnormal thickenings, tender spots or places where glands are enlarged, softened, or hardened. When gonococci cannot be found by microscopic methods culture may reveal their presence.

A single negative examination is by no means proof that gonococci are absent, as we have frequently failed to find them on two examinations and succeeded at the third attempt. The surgeon who relies merely on the absence of threads or cloudiness from the urine as a criterion of cure will be surprised to find in how many of his apparently cured cases gonococci can still be demonstrated by some such means as those we have described.

In examining the female genital tract, attention should be directed to the places where the gonococcus is most likely to lurk, and every effort made to obtain a specimen from these which is uncontaminated by the ordinary

bacterial flora of the vagina. As we have mentioned, the latter contains many Gram-negative bacteria, and it may not always be easy to make out the characteristic shape of the gonococcus in the multitudes of organisms to be found in a specimen containing vaginal discharge. The cervix should be isolated by means of a speculum, and it is well to remove the discharge as much as possible with swabs, taking the specimen from the surface of the cleaned mucous membrane. Cultures have often succeeded where microscopic methods alone have failed to reveal the gonococcus in the female tract.

In gonorrhoeal arthritis puncture of the joint and removal of some of the fluid in it will often succeed in finding the gonococcus, either microscopically or by culture, but the puncture must be done sufficiently early, as gonococci seem to disappear from the joint fluid after about the sixth day. In gonorrhoeal endocarditis blood culture may be successful in demonstrating the nature of the lesion. Serological methods have not so far been much used in the diagnosis of

gonococcal metastases, though Müller and Oppenheim, Bruck and others have shown that complement is bound when brought into contact with the blood-serum of these cases and extract of gonococcus. Our work in this direction has confirmed the results of these authors, but whether the test is sufficiently specific to be of use as a diagnostic measure cannot be stated at present.

CHAPTER III

VACCINE AND SERUM THERAPY

Vaccines.—As is well known in many other bacterial infections, the subcutaneous injection of the dead bodies of the specific bacteria is frequently attended by the happiest results, and it is natural that much should be hoped from a similar procedure in the case of gonococcal infections. This hope has been largely fulfilled with regard to the complications of gonorrhoea, if we may judge from the literature and our own experience, though no great success has attended the use of gonococcal vaccines in attempting to shorten the acute stages of gonorrhoea. Probably there is no bacterial disease in which one can obtain such brilliant results on occasion as in gonorrhoeal arthritis. In too many cases to make it accountable by mere coincidence we have seen the injection of an appropriate dose of

gonococcal vaccine followed by complete relief of the patient's symptoms in the course of a single day. One would have to detail the histories of many such cases to convince the sceptic that the rapid benefit which had followed the injection of vaccine was not due to mere coincidence, but the following, which occurred in our own experience, is instructive.

A patient was admitted to the ward of a colleague suffering from very severe gonorrhoeal arthritis and acute gonorrhoea. On account of its difficulties, local treatment of the gonorrhoea was not administered at first. During the course of the following ten days no improvement occurred and, after a consultation with one of us, urethral injections were commenced, and a dose of gonococcal vaccine (25 millions) administered hypodermically. The following day our colleague, who had no great belief in the value of vaccine treatment, announced that he had never seen such marvellous improvement occur in a case of gonorrhoeal arthritis as had followed irrigation of the urethra in this case; practically all pain had disappeared, and the

temperature was normal. The irrigations were continued, but twelve days later the arthritis returned. Another dose of vaccine was administered, and its effect was as rapid as in the first instance.

Though vaccine acts so rapidly in many cases of gonorrhoeal arthritis, a few doses sufficing to effect a complete cure, we have had others in which its effect was not so marked, and in some of these it is doubtful whether it did any good at all. Probably our experience in this respect coincides with that of others, since in the literature one finds it often stated that from one to eight doses of vaccine were given at intervals of five to eight days.

Our own cases of this description seem to be divided into three classes. In the first, the patient is apparently overwhelmed with the gonococcus and its toxin; one joint after another becomes affected, there is sustained high temperature and often a cardiac bruit. In some of these the injection of vaccine is followed by rapid improvement, but in others, though some slight improvement often occurs, as shown by a fall

of one or two degrees in the temperature and some relief in the pain following each injection of the vaccine, recovery does not take place for many weeks, or even months. The second class comprises subacute cases with considerable periarticular thickening. The improvement under vaccine is very slow and spread out over weeks, so that we may come to doubt whether the treatment has any effect at all. If, however, vaccine treatment be suspended in this belief, the arthritis becomes more severe, and we are bound to conclude that, even if it is slow, vaccine therapy is of distinct value in such cases. It is probable that in these patients the sclerosing process has advanced so much that, as Sir A. E. Wright points out, the lymph stream through the diseased area is not adequate to carry the antigonococcal substances to the micro-organisms in the part; some such adjuvant as Bier's treatment may be useful in such cases. In the last class of cases, to which we would refer, the symptoms are due more to joint deformity resulting from the gonococcal infection than to any active gonococcal inflammation. Most of our

cases of this kind have had considerable thickening round the insertion of the tendo Achillis and of the plantar ligaments, while the patient has often become flat-footed owing to the weakened plantar ligaments having given way under his weight. In these cases vaccine treatment may do a little good, and we believe it should always be persevered in with the object of stopping any further changes due to the action of the gonococcus, but it cannot be expected to repair anatomical deformities. In early cases of gonorrhoeal epididymitis the beneficial effects of vaccine treatment are generally well marked; when administered early it frequently produces rapid relief, and in older cases with extensive infiltration we have frequently found that after persevering with vaccine treatment for some weeks the thickening has completely disappeared as far as could be ascertained by palpation. In other gonococcal metastases, particularly iritis, good results have been reported from time to time by various authors.

In gonococcal infections of the mucous membranes, especially in acute gonorrhoea, the

general belief is that vaccine treatment is not indicated, as it has no effect in cutting short the disease. In the vulvo-vaginitis of little girls, however, Hamilton and Cook, as well as Butler and Long, report good results from vaccine, especially in the chronic stages. The former found no particular benefit from local treatment, and their later cases were all treated with vaccine only.

In the case of gonorrhoeal urethritis we can confirm the statement that the use of vaccine has no effect in cutting short the acute stages of the attack, judging this from the duration of the purulent discharge. For a time we administered a dose of gonococcal vaccine to every alternate case of gonorrhoea on admission to the hospital with which we were connected, and then took an average of the number of days spent in hospital by each of the two classes of cases. It occurred to us, however, that even if the use of vaccine had little effect on the gonococcus when the latter was growing on its optimum medium, the excellent effects which followed its use in gonorrhoeal arthritis, and similar

complications, gave grounds for hope that if the antigonococcal substances in the patient's blood were increased by administering vaccine, any gonococci which trespassed beyond the limits of the urethral mucous membrane would be destroyed at once, and no complications occur.

The investigation just referred to was of no use for the purpose of testing this, as certain essential facts were missing from the case records, so another series was commenced in which a dose of vaccine was given to every alternate case of gonorrhoea which was not at the time suffering from a complication, or any other disease, on the day of admission. In every case the diagnosis was established by means of the microscope as well as clinical signs. The patients then passed on to the care of another medical officer, who treated both classes identically.

This investigation had not proceeded very far when it was unfortunately interrupted, and we can only say that the results were encouraging. We mention them here as they suggest an important use for vaccines in gonorrhoea.

In all, eighty-four patients were admitted during the investigation; to forty-two of these a dose of vaccine (25 millions) was given on admission, and to forty-two, no vaccine at any time, unless complications occurred. Of the patients treated with vaccine, four subsequently developed epididymitis, including one who developed this complication eighteen hours after the injection. Of those who were not treated with vaccine, ten developed epididymitis, and one of these suffered also from very severe arthritis. Lieut. C. H. Harold's very careful notes on all the cases showed that in those treated with vaccine periurethral thickenings were not so marked, and the general course of the urethritis was milder, though the duration of the purulent stage was not markedly affected. In many of the cases an increase of the discharge, lasting a day, appeared to follow the vaccine, but there was no marked exacerbation of symptoms nor any untoward incident which would contraindicate its use in such cases.

Preparation of Vaccines.—Having obtained 24-hour, or younger, growths of gonococci from

two or three sources on Wertheim's, or other suitable medium, they are washed off with a little sterile salt solution (0·85 per cent.). We have found the most convenient way of doing this is to draw a little of the salt solution into the bulb of a sterile chambered pipette and force it repeatedly over the surface of the medium till it has carried away as much of the growth as possible. Having obtained a fairly turbid emulsion in this way, it is transferred to a sterile test-tube, and the next task is to break up the clumps of gonococci into separate diplococci. In the absence of a mechanical shaker, this can be do in the following way:—

A sterile capillary pipette is cut off squarely at its lower end, and the barrel part armed with a rubber teat. The end of the pipette is then pressed firmly against the lower end of the test tube and the emulsion forced in and out of the pipette many times till it appears quite uniform. The clumps of gonococci passing between the sharp edge of the pipette and the bottom of the test-tube are gradually torn asunder. This is rather a tedious process to carry out, but it is

essential to have a uniform emulsion for accurate standardization.

The standardization can be done in various ways. We generally count the cocci by Wright's method and by Leith Murray's. To carry out the former the finger is pricked, and a volume of blood drawn into a capillary pipette, then one or two volumes of the emulsion, according to its thickness, and, lastly, a few volumes of normal salt solution. The whole are then well mixed and a drop of the mixture spread on a microscope slide by means of another slide, the corners of which have been broken off, in such a manner as to produce a film the edges of which lie well within the borders of the slide. The film is then allowed to dry and stained by Leishman's or other suitable blood stain. In counting, it is a great convenience to have some device by which a more or less square area of the field can be sharply delimited, and the simplest way of doing this is to cut out a circular piece of cardboard to fit inside the eye-piece of the microscope and rest on the diaphragm. A hole is made in the cardboard the size of the

diaphragm's opening, and to its border are fixed with sealing wax four fine glass filaments arranged in such a way as to include a small square in the centre of the hole in the cardboard. Using such a device, a hundred fields are examined in different parts of the film and the number of red cells and of cocci respectively included in the central square area of each are counted. The respective totals are then ascertained, and the calculation made as follows:—

$$\text{Total red cells} : \frac{\text{Total cocci number}}{\text{number of volumes of emulsion in the mixture}} :: 5{,}000{,}000{,}000 : 1$$

The number of cocci per c.c. in the emulsion.

Leith Murray's method is as follows:—The emulsion is counted in a haemocytometer, as if it were a sample of blood, the diluting fluid being made according to the formula given in the appendix or a 0·3% solution of some simple stain such as methylene blue. After making the dilution in the usual way, as for red blood cells, and transferring a drop to the table of the haemocytometer,

[1] For greater accuracy a red cell count can be previously made, but for all practical purposes it is sufficient to reckon this as 5,000 millions per c.c.

it is covered with a No. 1 cover slip, and the specimen allowed to stand for at least half an hour to allow the organisms to take up the stain. The count is made with a $\frac{1}{12}$ in. objective, and the calculation is the same as in counting red cells in blood. It is difficult to obtain an accurate count of gonococci, as degenerated forms stain badly and may easily be missed. To avoid this as far as possible, the growth from which the vaccine is made should not be older than twenty-four hours.

After counting the vaccine it is killed and diluted to a convenient strength. This can most conveniently be done by the addition of 0·5 per cent. carbolic or 0·25 per cent lysol. Heating is not necessary, and we think it interferes with the efficacy of the vaccine.

Dosage and Method of Administration.—It is very difficult to give precise directions on this point. Some authors have had excellent results from doses of $\frac{1}{2}$ to 5 millions given every three days, while others consider 50 millions a very small dose and recommend a gradual increase from 200 to 1,000 millions, with intervals

of from five to eight days. Probably the reason for this very great variation in the doses employed by separate workers lies in the different methods of preparing the vaccines which were used by each. Other things being equal, a vaccine prepared from a recently isolated strain is more toxic than one which has been subcultured for many months, while a vaccine which has been killed by heating is less toxic than one which has not been heated. Naturally, the more toxic the vaccine, the less the dose of it which can be given with safety, so that workers who used a recently isolated strain and did not employ heat to kill it would find themselves compelled to give considerably smaller doses than those who prepared their vaccines from old strains which had been killed by heating. Direct support for this is found in Eyre and Stewart's observations. These workers found that when they used old strains they had to give doses of from 100 millions to 500 millions to obtain any immunizing response; now that they employ cultures of recently isolated organisms they strongly recommend great caution, and frequently commence with a dose

of 500,000, increasing this gradually to 5 millions or 10 millions, and practically never exceed 25 millions. Their vaccine is heated at 50°C. for a total of 1½ hours, which is not likely to affect its toxicity very markedly. Hamilton and Cook, treating the vulvo-vaginitis of little girls did not obtain such good results with recently isolated as with older strains. They gave doses of from 5 millions to 10 millions, increasing to 25 millions, and it is possible that if they had reduced the dose when using the recently isolated strains their results would have been better than those they actually obtained with the latter.

As to the respective therapeutic merits of vaccines prepared from recently isolated and from older cultures, we do not think enough work has been done on the subject to justify a definite opinion. Eyre and Stewart consider that the recently isolated are more potent therapeutically, but their work still leaves us unconvinced that virulence and immunizing power run *pari passu*. In the case of other bacteria, we know that they do not in typhoid. The typhoid vaccine

for the Army is prepared from a strain which was isolated more than ten years ago. It has become quite avirulent for animals, but its immunizing power on man has been proved by long and patient investigation to be superior to that of any recently isolated strain yet tested at the Royal Army Medical College. In this case, apparently, it is not the age of the strain, but some other property, which affects the immunizing power of the vaccine. A disadvantage of using a very toxic vaccine is that the margin of safety is so narrow. This would not matter very materially if one could rely on absolutely accurate standardization, but in the case of the gonococcus we do not believe this is possible with any method which is known at present. For these reasons, we prepare our vaccine from strains which have been subcultured many times. At the same time we do not use heat to kill it, as we think that heating materially lessens its immunizing power.

Regarding the use of the opsonic index as a guide to the administration, most workers say that it is desirable, though not absolutely essen-

tial. For ourselves, we confess that in the majority of our cases we have dispensed with its assistance. From a number of estimations which we made, we found it particularly difficult, if not impossible, to obtain reliable results when working with the gonococcus. Even with reasonable care it is impossible to prepare an emulsion which does not contain many involuted cocci, and these not only stain badly, but are indistinguishable from broken-up blood cells, which can be phagocyted, so that large numbers of leucocytes must be counted before an approximately accurate estimate can be made. Altogether, therefore, as we propose to use vaccine in all stages of gonococcal infections, and have, so far, no particular reason to be dissatisfied with our results, we do not see any advantage in adding the toil and eye-strain of innumerable opsonic determinations to our other labours.

Most workers agree that a stock vaccine prepared from a number of different strains is practically as good as one made from the patient's own organisms. The use of an autogenous vaccine may therefore be reserved for those cases

which do not progress satisfactorily under treatment with the stock vaccine.

Based on the above considerations, our practice varies with circumstances. When a new batch of vaccine has been prepared we give a dose of (approximately) 12½ millions to some mild case of gonorrhoeal arthritis, or of epididymitis, and watch its effect on the local and general symptoms. If these are not increased, but little benefit results, the next dose, given a week later, is increased to 25 millions, and this amount is given initially to all future cases of the same kind. Severe reaction is an indication to reduce the next dose. We give larger doses to cases of arthritis where the symptoms are subacute or chronic, and gradually increase them at weekly intervals to 100 millions. When the patient is acutely ill, and the whole train of symptoms points to very extensive infection, we commence with a dose of 5 millions and watch its effect on the temperature and general symptoms. If these are unaffected, the dose is increased to 10 millions after three or four days. Thereafter the dosage is regulated by the general

signs. We attach considerable importance to absolute rest of the affected joints in these cases ; apart from the loss of sleep entailed by the constant liability of unfixed joints to movement, it is probable that the patient receives considerable amounts of the poison by auto-inoculation when he is not kept completely at rest.

In acute gonorrhoea we have usually given 25 millions at weekly intervals. In chronic gonorrhoea we increase the dose gradually till it produces a distinct increase of the discharge. In these cases it is necessary to remember that other organisms may be keeping up the inflammation, and a vaccine prepared from any of these which may be isolated and are known to be pathogenic may be advisable.

Serum Therapy. — In 1906, Rogers and Torrey announced that they had obtained excellent results from the injection of antigonococcal serum in the complications of gonorrhoea. The serum was obtained from rams which had been injected with repeated doses of gonococcus emulsion, and was administered subcutaneously in a dose of from 2 to 6 c.c. every alternate day,

or at longer intervals, according to the reaction following each injection. From their reports, and those of other workers who have tried this serum, its immediate effect in most cases was some local redness, and possibly a transient increase of the patient's symptoms. In a few other cases (10 out of 75 of Rogers' and Torrey's patients) symptoms of the nature of serum sickness followed the injection very quickly, these being sometimes very alarming. There was a feeling of suffocation with very feeble, rapid pulse and a general erythematous rash, the patient being very prostrated. In cases prone to develop these symptoms, the latter seemed to be more severe with each successive injection. The serum has no effect on urethritis, but it is claimed for it that in the majority of cases epididymitis clears up after one or two injections, and arthritis after three or four. Torrey's serum is sold by Parke, Davis & Co. A serum made by Burroughs, Wellcome & Co. is given in larger doses, and excellent results are reported by some workers with it, but we have no practical experience of its effect.

Personally, we are disinclined to use serum in any disease unless there is no alternative, as in diphtheria, because of the occasional risk of severe serum sickness, such as we have described above. It may not matter so much at the time, but some patients are made specially sensitive to the action of serum by the administration of one dose, and this sensitiveness may last for three or four weeks. If such a patient were to contract diphtheria within this time the administration of antidiphtheritic serum might result in dangerous symptoms. We prefer, therefore, to trust to vaccines, which appear to us to be as effective as, if not better than, serum.

CHAPTER IV

PRIMARY INFECTIONS

The usual seats of primary infection are—

1. The male urethra.
2. The female urethra and cervix uteri.
3. The conjunctivae.
4. The vulva in little children.

Other primary infections which have been described are those of the mouth and anus. Infections of the buccal mucous membranes are extremely rare and in most of the reported cases the patients were newly-born children. Primary infections of the anal mucous membrane have been reported in males as the result of unnatural practices, but most of the infections occur in females and are caused by a gonococcal discharge from the vagina.

Gonococcal Infections of the Male Urethra.—When the gonococcus effects a lodgment in

the male urethra the result is a specific urethritis commonly known as gonorrhoea and also by a number of more vulgar terms.

The course of the urethritis is largely influenced by the anatomical boundaries of the canal and these must first be briefly considered.

ANATOMY.—From a gonorrhoeal point of view the male urethra consists of an anterior portion separated from the posterior portion by the compressor urethrae. This muscle acts as a sphincter and is very powerful for its size, requiring in most cases a pressure equal to that of a column of water five feet in height to overcome its resistance. It follows therefore that any secretion formed in the anterior portion of the urethra must flow towards the meatus, as it cannot pass backwards, and conversely that any secretion visible at the meatus must have come from the anterior portion. Pus secreted by the short posterior portion cannot pass the sphincter but accumulates in the posterior portion and if of sufficient quantity reaches the bladder, mingling with the lowest layers of the urine there (*see* Two Glass Test, page 105).

The second point of interest is the epithelial lining of the urethra. At the meatus and in the fossa navicularis the epithelium is of the squamous variety; from this point up to the compressor urethrae the canal is lined with cylindrical epithelium, while the remaining portion has squamous epithelium on its floor and the transitional variety on its upper surface. The epithelial lining rests on a layer of connective tissue containing many elastic fibres which run into the erectile tissue and so doubtless furnish an anastomosis between the subepithelial lymph spaces of the mucosa and those of the erectile tissue.

The last point which has to be borne in mind is in connexion with the follicles and glands whose ducts open into the urethra. In the upper wall of the anterior portion of the urethra there are some twenty follicles, the lacunae of Morgagni; these are really indentations of the mucous membrane lining the canal. Much more important are the glands of Littré which are scattered over the whole surface of the urethra. They vary considerably in size and development, the largest being found along the middle

line of the upper surface of the penile portion. They are lined with cylindrical epithelium.

Next in importance are Cowper's glands which lie between the layers of the triangular ligament and open into the floor of the urethra at the commencement of the bulbous portion. In the posterior portion we have the orifices of the ejaculatory and prostatic ducts opening into the urethra at the caput gallinaginis; these ducts play a most important part in the persistence of gonorrhoea as well as in permitting extensions of the disease to surrounding parts.

Path of Infection.—The exact method by which the gonococci gain admission to the urethra is not quite clear. During coitus the meatus is tightly closed and any cocci which happen to come into contact with the meatus should be swept away by the act of emission. Immediately after coitus has been completed the meatus is relaxed and it is possible that gonococci which have adhered to its sides may gain entrance to the urethra at this time; or they may adhere to the adjacent surfaces of the prepuce and glans penis, being subsequently intro-

duced into the urethra by the movements of the body causing the prepuce to play over the glans. Some such explanation would appear necessary to account for the great difference in time in different cases between the exposure to infection and the development of symptoms of the disease, as this is hardly likely to be entirely due to the different resisting powers of individuals.

Clinical Types of Gonorrhœa.—Gonococcal infections of the urethra vary in their severity according to the virulence of the infecting strain and the resistance of their host; the patients may also present themselves at different stages of the disease so that clinically we meet with four fairly distinct types of the disease.

1. The extremely acute form. This is fortunately of somewhat rare occurrence. The few cases which we have seen have been in young lads with fair hair and fresh complexions. The patient looks ill and generally has some pyrexia. There is a copious urethral discharge of creamy yellow or greenish yellow pus, sometimes stained with blood; the penis is swollen, the prepuce and glans are red and inflamed, while micturition

is extremely painful. In two cases there was temporary retention apparently due to tenesmus of the sphincter. The urine when seen in a glass is turbid and loaded with pus.

2. The ordinary acute case, in which there is a free purulent discharge and micturition is exquisitely painful but there is little constitutional disturbance; the urine is turbid.

3. The subacute case in which there is a slight muco-purulent discharge but no other discomfort. The urine is hazy, i.e. not thick and turbid as in the acute case but yet not quite clear.

4. The chronic case. In this there is no visible discharge, or at most a thin mucoid drop at the meatus in the morning, commonly called a gleet. The urine is clear but contains threads and mucus.

The Symptoms and Diagnosis of a Gonococcal Infection of the Male Urethra.— Every gonococcal infection is accompanied by more or less inflammation according to the severity of the infection and the time the infection has lasted. If the gonococci can be demonstrated in the urethral discharge either by means of stained specimens or by cultures

obtained from the secretion the diagnosis is established. If for any reason these methods cannot be employed we must fall back on the clinical symptoms and history of the case. The first clinical signs of the disease usually appear in from three to five days after the infection has taken place although the time may be much longer, and in some recorded cases has even been as long as thirty days. The earliest signs are: a slight sensation of tickling in the urethra, especially on micturition, the lips of the meatus have a tendency to stick together and on first rising in the morning a bead of mucopurulent secretion may be noticed at the meatus. The inflammation quickly increases in severity and the desire to micturate becomes frequent and urgent, the act being more or less painful, often excruciatingly so. Soon a thick purulent discharge makes its appearance and the disease is then well established. The patient, especially if the attack is at all severe and is a first one, soon begins to feel out of sorts and may have a little fever in the evening. When the acute stage has lasted for some three to ten days, or occasionally longer, the

inflammation begins to subside and a subacute stage is reached in which the pain on micturition is slight or absent, the discharge diminishes in quantity, becomes mucopurulent and finally mucoid and only visible in the morning. This may last from a month to six weeks, when the chronic stage is reached. In this stage there are practically no symptoms except an occasional bead of discharge in the morning, but if the patient indulges too freely in alcohol or sexual intercourse a relapse is almost sure to take place.

Something like 99 per cent. of the cases of urethritis are due to the gonococcus, sometimes associated with other cocci it is true. If therefore a painful purulent urethritis appears in a young man for which there is no obvious cause, such as the passage of an infected instrument, we are not likely to be far wrong in calling it a gonococcal infection, and unless some medico-legal question depends on the diagnosis, it matters little to the patient whether we ascribe his disease to a strepto-, a gono- or any other kind of coccus. As a matter of experience the young male adult usually makes his own diag-

nosis, merely consulting his doctor on the question of treatment, and not even always on that. The extent to which the urethra has become infected may be roughly gauged by applying the "two glass" test.

The Two Glass Test.—The test should be applied to the urine passed on rising in the morning, as this contains the pus secreted during the whole of the preceding night, whereas during the day when the patient is taking much fluid and emptying his bladder at fairly frequent intervals, the pus secreted during the intervals between micturition is so much diluted that it may escape detection. The test is carried out by making the patient pass about 4 ounces of urine into one glass and the remainder into the second. The first glass therefore contains urine which has come from the bladder and en route has washed out the anterior urethra. If the urine in the bladder is normal any pus in the first glass must have come from the anterior urethra. Unfortunately the urine in the bladder may also contain some pus, especially the lower layers of the contents, and in this way

an early posterior urethritis may be overlooked. If it is desired to eliminate this fallacy the anterior urethra must first be well washed out with sterile water and the test then applied. The first glass will then contain the urine which has been in contact with the posterior urethra and base of the bladder, while the second glass will contain the urine from the body of the bladder. In this way the presence of a general cystitis may be detected. The test can at best only be regarded as approximate in so far as the extent of the urethritis is to be judged by it.

The results of the test may be tabulated as follows:

First Glass.	Second Glass.	Condition.
Turbid . .	Clear . .	Acute anterior urethritis
Turbid . .	Turbid . .	Acute anterior + posterior urethritis
Hazy . .	Clear . .	Subacute anterior urethritis
Hazy . .	Hazy . .	Subacute anterior + posterior urethritis
Clear, mucus and threads	Clear . .	Chronic anterior urethritis
Clear, mucus and threads	Clear, mucus and threads	Chronic anterior + posterior urethritis

The urine should be examined daily by this test as it affords a useful indication as to the progress of the disease; it is most important that the urine examined should be passed at the same time each day, for if that examined one day is the first morning urine and the specimen seen next day has been passed at a later hour the surgeon may, owing to the greater dilution of the second specimen, come to the wrong conclusion that a great improvement has taken place.

When the chronic stage is reached one glass is really sufficient, as in practically every case the gonococci reach the posterior urethra and once there they adopt the motto "J'y suis, j'y reste."

The Endoscope or Urethroscope.—During the acute stage the endoscope should not be used and is indeed quite unnecessary, the introduction of a hard metal instrument can only do harm and is quite unjustifiable. In the chronic stage, especially when a gleet obstinately refuses to clear up, the endoscope may at times reveal some simple and easily remediable cause. A certain amount of practice is necessary in order

to be able to interpret the various appearances met with.

Many different patterns of endoscope have been introduced and each possesses its own special advantages. In some, e.g. Leiter's, Hurry Fenwick's, Wyndham Powell's, a reflected light is employed, the lamp being situated outside the urethra and the light thrown down the canal by a mirror or a prism as in Pardoe's urethroscope. These patterns do not give such a good illumination of the part as those in which the lamp is placed in the cannula, but have the advantage that the urethra can be inflated or that operative work can be carried out through the tube while the operator sees what he is doing. In Valentine's and Luy's endoscopes the light is furnished by a minute electric lamp on a stylet placed at the extremity of the cannula. This gives an excellent illumination, as the lamp is close to the part which is being examined. The cannula is, however, sharp, and constant care must be exercised not to allow the instrument to rest on the mucous membrane, as the sharp edge of the cannula will readily cause a wound of this

structure. Wossidlo has a specially curved endoscope which can be passed into the posterior urethra; when in position a shutter can be opened and a view of the caput gallinaginis obtained.

TECHNIQUE.—Whatever instrument is used it must first be passed into the urethra for its full length and the stylet withdrawn. A minute pledget of cotton wool is then fixed in the catch of the special probe supplied with the instrument and passed down to the end of the cannula to take up the pus and mucous secretion which is always present. This should be repeated till the wool comes up dry.

If Valentine's pattern is being used the light holder is then inserted and clamped in position without exercising any pressure on the cannula. The electric current is then turned on and the resistance adjusted so as to give a good illumination. The urethra can then be examined, always remembering that the cannula can only be withdrawn and that the urethra must be examined in the direction from behind forwards; if the surgeon wishes to re-examine a portion of the

mucous membrane posterior to that at which the end of the instrument is, he must withdraw the lamp-holder, reinsert the stylet and pass the endoscope into the urethra again.

Leiter's pattern has a blunt-edged cannula and it can therefore be pushed gently backwards without reinserting the stylet.

The colour of the normal urethra varies according to the vascularity of the mucous membrane, and differs in different individuals and in the different parts of the canal; the navicular fossa is, as a rule, pale pink and the rest of the urethra a rosy pink. In a healthy urethra the mucous membrane collapses immediately beyond the end of the cannula, so that on looking down it a number of fine rugae are seen radiating outwards from the centre to the periphery. In a diseased urethra the conditions which may be met with are: Soft infiltrations, hard infiltrations, stricture, erosions, ulcers, granular patches, inflamed follicles, minute cysts and deposits resulting from certain drugs.

Soft infiltrations. These are due to a plastic infiltration of the submucous tissue. When

present the mucous membrane instead of presenting the appearance of a crimson rosette, suggesting the badge of some foreign order, shows a bulging shiny smooth red surface cut up by several deep sulci into uneven portions. When this condition has advanced a little further it is called a hard infiltration; in this condition the mucous membrane fails to collapse and a space is left in the centre. When the condition has progressed so far as to be called a stricture the canal remains quite patent, the divisions are more irregular and the surface is pale and rough.

Erosions are recognized by their rough surface and liability to bleed; ulcers have a yellowish or grayish surface with some pus adhering to it. Granulations are not infrequent and are obvious.

Inflamed follicles may be seen as minute rosebuds with possibly a point of pus showing. They are so small that unless distended with secretion or much inflamed any abnormality may easily escape notice.

Cysts are rare and only detected when a follicle is occluded and becomes distended with mucoid secretion.

Zinc, lead and bismuth may give rise to chalk-like deposits; silver salts may leave yellow stains.

Prognosis.—The prognosis of gonorrhoea in the male, as far as danger to life is concerned, is distinctly good, as a fatal result only occurs in exceptional cases when the gonococcus as a result of metastasis attacks some important organ like the heart.

As regards the question of cure it is impossible to give a definite answer which will apply to all cases. If the patient is seen within forty-eight hours of contracting the infection we may by adopting vigorous methods be able to cure him in a week to ten days, but this is by no means certain. Usually the patient does not begin treatment till the acute stage has become fully developed. Under these circumstances the most hopeful prognosis which we can give is that, by conscientiously carrying out the instructions given him, and with ordinary luck, the discharge may cease in about six weeks, but that this does not guarantee that he is cured, and

that in any case he must lead a most careful and regular life, avoiding all excesses, for at least another six months. At the same time the patient must be clearly informed that in many cases gonorrhoeal urethritis persists in a chronic form for years, and the possibilities of uncured gonorrhoea should be impressed on him.

The prophylaxis has been sufficiently discussed in the introductory chapter.

Before discussing the treatment of gonorrhoea in the next chapter it is advisable to refer briefly to the pathology of the disease.

Gonorrhoea is an infective disease caused by the gonococcus and characterized by an initial acute inflammation, followed in most cases by a subacute and chronic stage, the latter of which tends to persist for a long period. During the first twenty-four hours the gonococci are on the surface of the mucous membrane and in this position may easily be destroyed. Very soon they grow downwards into the intercpithelial spaces and at the same time invade the numerous glands and ducts which open into the urethra. When the gono-

cocci have reached these positions it is hopeless to attempt to destroy them; the treatment should therefore be mainly directed to washing away the gonococci, toxin and inflammatory exudation which if allowed to remain on the surface of the mucous membrane tend to prolong the acute stage of the disease.

The practical application of the above is that if the patient is seen in the early stage of the attack, strong bactericidal solutions may be used in the hope of killing the gonococci before they have penetrated to the deeper layers. When the acute stage has become fully developed only weak solutions should be employed, but in large quantities. In the chronic stage there is little or no exudation, hence local treatment is of little or no use and the best results are to be obtained by improving the patient's general health.

CHAPTER V

TREATMENT OF GONORRHOEA IN THE MALE

THE treatment of gonorrhoea may be most conveniently considered under the following headings :—

I. The general management of the case.

II. Medicaments administered internally.

III. Vaccines and drugs administered hypodermically.

IV. Urethral medication.

I. The General Management of the Case.—The general management of the case comprises the questions of rest, diet and baths.

REST.—All gonococcal infections are accompanied by more or less inflammation, hence the old surgical maxim of resting an inflamed part should be adhered to, but with special reservations to suit the circumstances of the case. Most writers advise that a patient suffering from

acute gonorrhoea should be kept in bed. If the attack is extremely acute and the patient is suffering from very severe pain this advice is sound, but in the ordinary acute case keeping a healthy young adult in bed is attended with certain objections. The position soon becomes extremely irksome and the patient is very liable to suffer from dyspepsia, flatulence and constipation owing to the want of his usual exercise. In the next place the genital organs are kept permanently in a much warmer atmosphere than they are accustomed to during the day-time and this has a great tendency to induce nocturnal erections; each erection during the acute stage prolongs the duration of the attack by about a week and increases the liability to future complications.

When considering the question of "rest," therefore, we ought to remember that our object is to give the inflamed urethra as much rest as possible without interfering with the general health. The best way of accomplishing this is to get the patient out of bed and either let him lie on a sofa or sit in

an armchair, if possible out of doors; he should also be permitted to stroll about whenever he finds his position tiresome. Any kind of physical exertion should be avoided; cycling, horse exercise, rapid walking and sitting in a jolting vehicle, should be forbidden.

Once the gonorrhoea has become thoroughly established our best weapon for fighting it is the patient's own powers of resistance to the gonococcus; by keeping him in bed to brood over the progress of the disease we will almost certainly lower his resistance. On the other hand, by allowing him to spend a good deal of his time in the open air where he can see his fellow-creatures and find something to interest him besides his own symptoms, we improve his health and so increase his resistance.

The patient should sleep on a firm bed, retire early and rise somewhat later than usual. During the acute stage of the disease he should remain at home, but if obliged to continue at work he must take life as easily as possible and pay for "taxis" instead of strap-hanging in tubes or running after motor omnibuses in motion. In

the subacute stage walking exercise to a mild extent may be taken. In the chronic stage the more out-door exercise the patient can take the sooner he is likely to become apparently cured. Soldiers who carry out the instructions given them, especially in regard to the abstinence from alcohol, get well more quickly when sent to duty than when kept in hospital.

DIET.—In the acute stage the urethra is inflamed, congested and exquisitely tender; we should therefore prescribe a diet which will render the urine as little irritating as possible. The first step towards accomplishing this is to make the urine dilute by ordering the patient to drink large quantities of fluid, especially milk mixed with barley water, soda water or any natural alkaline water. Aerated waters are not usually recommended in text books: we do not know of any objection to their use and have always prescribed them freely. Similarly tea and coffee are not advised, but if partaken of in weak infusions, or used to flavour the milk, which when taken plain soon nauseates the patient, there cannot be any real objection to

their use. Porridge and other cereals, fresh vegetables, white fish, mutton or chicken broth, if not made too concentrated, may all be allowed in order to vary slightly the somewhat monotonous diet of milk which should constitute the principal food during this stage of the disease. Red meats, spices, acid fruits and vegetables should not be permitted, and alcohol in any form must be absolutely forbidden.

When the subacute stage is reached the diet should be gradually increased, spices, acids and alcohol being still prohibited. We must remember that the patient's system has been subjected to a considerable drain and that consequently he requires feeding up. By insisting on a low diet at this stage of the disease we retard his recovery instead of hastening it.

During the chronic stage the patient should have a liberal diet without alcohol.

In regard to the use of alcohol, some of the German writers actually prescribe it during the acute stage with the idea of increasing the urethral discharge and so stimulating the ex-

trusion of gonococci. This view is not generally accepted.

Baths.—In the rare extremely acute form of the disease a continuous hot bath is undoubtedly a most useful form of treatment. It is somewhat difficult to carry out unless the hospital happens to possess a bath fitted up for the purpose. An apparatus for a continuous hot bath may be improvised in the following way: A sitz bath is filled with hot water and propped up on bricks, a spirit lamp being kept burning underneath to maintain the temperature of the water. The patient is placed in the bath with an air cushion to protect his back and another for his head, or if this is not available, a pad must be arranged by folding up bath towels and placing them on the parts which are subjected to pressure. A blanket must then be placed round the patient's body and shoulders. In this way a patient can be kept in a continuous hot bath for some twelve hours, or even longer.

In the ordinary acute case prolonged hot baths are very comforting and may exercise a mildly beneficial influence on the course of the disease.

When a patient with a gonorrhoeal discharge is ordered any form of bath treatment, he must be specially cautioned as to the danger of infecting his eyes, as the gonococci retain their virulence as long as they remain moist.

II. **Drugs Administered Internally.**—These may be divided into (1) Sedatives, (2) Balsams, (3) Antiseptics.

The sedatives include opium, belladonna, hyoscyamus, stramonium, uva ursi, buchu and pareira; for practical purposes we may also include the alkaline carbonates and citrates, as although strictly speaking they do not belong to the group of urinary sedatives yet in treating gonorrhoea we employ them to render the urine less irritating, so that their action is really that of a sedative. As to the individual drugs, opium is not generally employed internally as it has the disadvantage of upsetting the patient's digestive system, while its action on the urinary tract is only a small part of its effect on the central nervous system. In the form of a suppository it is however a most useful sedative in acute and painful cases.

Of the others, hyoscyamus and buchu are most commonly employed in this country during the acute stage. They are supposed to exert a soothing influence on the inflamed mucous membrane of the urinary tract and possibly they may do so to a certain extent. The effect is, however, not very rapid or well marked, and we cannot say that we have noticed much difference in the symptoms of acute cases which were treated with these drugs as compared with those which merely received alkalies. Schindler uses suppositories containing 2 mgm. of atropine. He claims that the atropine inhibits the peristaltic contractions of the unstriped muscular fibres in the walls of the urethra, vas deferens and ducts opening into the urethra. Experience with atropine used in this way at the Military Hospital, Rochester Row, shows that it is not only a sedative but prevents the extension of the infection to neighbouring parts. It would certainly seem to be a much more effective way of employing the drug than the usual plan of giving small quantities of a tincture internally which can only exert an extremely mild

effect on the mucous membrane of the urethra.

The citrates and bicarbonates of sodium potassium and lithium and the carbonate of magnesium speedily render the urine alkaline, or at least greatly reduce its acidity, and should therefore be freely used in the acute stages. In the subacute and chronic stages they are of little value, while the carbonate of magnesium may, if continued for a long time, make the urine strongly alkaline and lead to the production of quantities of the large triple phosphate crystals; these irritate the surface of the urethra and exert anything but a beneficial effect.

2. The Balsams and Aromatic Oils.—This group includes copaiba, oil of sandal wood and oil of cubebs. The drugs belonging to this group are not usually administered till the acute stage has begun to subside as they are supposed to have a tendency to irritate the urinary mucous membrane when acutely inflamed. All three are very unpleasant to swallow and are inclined to upset the digestion; hence they should, if possible, be given in capsules. The active

principles are absorbed into the blood and excreted by the kidneys.

The quantity present at any one time must however be extremely small. It may be sufficient to act as a tonic to the mucous membrane but is not likely to have any effect on the gonococci lying snugly among the epithelial cells; moreover, as the principal seat of the disease is in the urethra, the greater portion of which lies outside the compressor urethra, the drug can only act on it during micturition, when the stream of urine comes into contact with the mucous membrane of the anterior urethra for a few seconds.

These drugs have been used in the treatment of gonorrhoea for many years, probably for centuries, and are still being used, which might be taken as conclusive evidence that they had proved their value for this purpose. The truth probably is, however, that the patient expects to be ordered one of them, and as the surgeon has nothing better to offer he complies with the patient's desire who then feels that he is really being treated

for gonorrhoea, especially when he happens to approach closely to any of his friends. There are also many expensive proprietary preparations of these drugs, e.g. arhovin, gonosan, santalin, for which the manufacturers claim numerous special virtues and back up their claims with glowing testimonials from patients and medical practitioners. We have no experience of their use, but they might easily prove to be superior to the balsams as usually prescribed.

3. ANTISEPTICS.—These include urotropin, salol, boric, benzoic and salicylic acids, as also many of their compounds. When the infection is purely a gonococcal one it is extremely doubtful if any of these drugs have any beneficial effect on the course of the disease; they do not do any harm and may possibly have some slight inhibitory effect on the growth of the gonococcus during the early stages of the disease. The quantity present in the urine at any one time must however be very small and it is highly improbable that such a weak solution passing rapidly over the surface of the mucous membrane could have any influence on the gonococci,

especially when these have penetrated to the deeper layers of the epithelium. In old chronic cases associated with stricture, and in which the bladder has been invaded by other pyogenic organisms, the antiseptics are most valuable, for in this case the germs are exposed to the almost continuous action of the drug as the urine accumulates in the bladder.

III. **Vaccines and other Drugs injected Hypodermically.**—This group includes (1) Vaccines, (2) Sera, (3) Colloidal preparations of silver.

1. VACCINES. The preparation and action of these have already been discussed (*see* Chap. III).

2. SERA.—The value of antigonococcal sera has been discussed in Chap. III.

3. COLLOIDAL PREPARATIONS OF SILVER.—Recently, collargol, a colloidal preparation of silver containing 86·6 per cent. of the metal, has been used either as a subcutaneous injection, 0·05 cgm. daily, or in the form of an inunction. Elektrargol is a still later preparation which is supposed to be more active and less irritating. Injections of

3 to 5 cc.s have been used with success in general gonococcal infection; in cases of epididymitis and arthritis local injections may be given.

IV. **Urethral Medication.**—There are two main schools holding diametrically opposed views on the question of urethral medication. One school, the "Symptomatic," hold that the inflamed urethra should be left severely alone till the inflammation has to a great extent subsided; the other, the "Antiseptic" school, teach that an attempt should be made at the earliest possible moment to destroy the gonococci by the introduction of bactericidal agents into the urethra. The "Antiseptic" school now has most adherents, many former members of the "Symptomatic" having seceded and joined the "Antiseptic" party.

The local treatment may be considered under the following headings:—(1) External applications, (2) Injections, (3) Irrigations, (4) Bougies, (5) Symbiosis, (6) Mechanical.

(1) External Applications.—In the hope of mitigating the inflammation various external applications have been made use of. Thus

in Germany a favourite practice is to apply an ice-bag to the penis; some practitioners prefer to soak the penis in hot water. The wearing of a suspensory bandage from the beginning of the disease is supposed to prevent the occurrence of epididymitis. These measures may afford some relief to the sufferer and by finding him some occupation may tend to produce a more contented state of mind, but it can hardly be maintained that they will appreciably affect the course of the disease.

(2) Injections.—In the lay mind injections are intimately associated with gonorrhoea and form part of the established ritual of treatment. From a medical point of view the object aimed at by employing injections is to bring an active medicament into intimate contact with the seat of the disease and so if possible destroy the gonococci. If a suitable agent is selected and the injections are employed within, say, twenty-four hours of the infection taking place there would be a very fair chance of obtaining a satisfactory result. When the patient presents himself for treatment the disease is usually well established and the

gonococci have penetrated the epithelial covering of the mucous membrane where they are amply protected from the action of any drug injected into the urethra. Injections given with the ordinary half-ounce syringe can only fill the anterior urethra or at most force a small quantity of fluid through the sphincter into the posterior urethra. Still, injections may be employed with benefit, even in acute cases, provided the solutions are not too strong or irritating. As it is useless to attempt the destruction of the gonococci in these cases the injections should be used with the object of washing away the gonococci, toxin and pus cells lying free in the urethra, hence a weak solution should be employed and frequently, at least once every four hours by day and if possible once or twice during the night. When the fluid has been injected it should be retained in the urethra for a few minutes and the penis lightly palpated during this time so as to make the fluid play over the whole urethral surface and detach any adherent flakes of pus.

After a very little instruction the patient may be entrusted to carry out his own injection, and

as he then feels that he is actively assisting to effect his cure he is much happier and less of a nuisance to his medical attendant.

Before using the injection the patient must be instructed to pass his water, and as this act washes away most of the infective matter lying in the urethra there is no necessity for compressing the root of the penis when making the injection: this practice would seem to be much more likely to assist the upward spread of the disease by detaching some of the colonies of gonococci from the urethral surface and forcing them both upwards and downwards. In any case our experience has been that the gonococci in the ordinary acute case always reach the posterior urethra eventually no matter what precautions are observed.

Apparatus.—The only apparatus necessary is a syringe having a capacity of roughly half an ounce, which quantity is just sufficient to fill the urethra without forcing any of the solution into the posterior urethra. The pattern of syringe usually employed has a long pointed nozzle which penetrates the urethra for some half

inch or even more. This is quite wrong as it is liable to damage the mucous membrane as well as to introduce a variety of germs each time it is used. The nozzle should be of a blunt cone shape or, better, a supply of blunt rubber nozzles should be kept, and one fitted to the syringe just before using it. The syringe and the cones, if these are used, should be disinfected after being used; this can be done by boiling or by soaking in a strong antiseptic solution for some hours, after which they should be washed in sterile salt solution and wrapped up in sterile gauze till required again.

There is another method of syringing which may be employed in the subacute stage, but which really offers few advantages, viz.: by using the large syringe. In this plan a syringe having a capacity of four to six ounces is used by the surgeon, who grasps the patient's penis with his left hand while holding the filled syringe with the second and third fingers of his right hand. He then presses the piston down with his thumb and sharply injects half an ounce of the solution at a time and immediately withdraws the syringe

to allow the fluid to escape; this manœuvre is repeated till the contents of the syringe are exhausted. The method is supposed to have the advantage of thoroughly distending the urethra and of bringing the solution into contact with every portion of the urethra. The objections to it are that it is very fatiguing for the medical man and that he can hardly avoid using a quite unnecessary amount of violence when making the injection. It also fails to effect its object, for no amount of pressure which a patient could tolerate will force any solution into the follicles or Littré's glands.

The posterior urethra and bladder may also be injected with the large syringe by merely keeping the syringe in position and maintaining the pressure. In this way it can be used as a substitute for irrigations.

Drugs.—A great variety of drugs have at one time or other been recommended for the treatment of gonorrhoea by injections. Few of these have stood the test of time, and those which are now employed may be grouped under the headings of (i) Antiseptics, (ii) Astringents.

(i) *Antiseptics.*—Perchloride of mercury, carbolic acid, picric acid, formalin and indeed almost every antiseptic substance has been tried, but practically the only ones now employed are permanganate of potassium and the newer salts of silver. Permanganate is hardly an antiseptic, as its action on the gonococcus is very feeble, but in the early stages it certainly seems to exert a beneficial effect on the course of the disease. It should always be employed in a weak solution—one eighth of a grain to an ounce of warm water; probably its beneficial action depends mainly on the slightly astringent influence which it exercises on the mucous membrane but it may possibly also produce some change in the toxins, rendering them less irritating.

Of the many organic salts of silver which have been introduced in recent years protargol, albargin and argyrol are the best known and most effective. Protargol contains 7·4 per cent. of silver and is more inclined to cause irritation than the others. The strength of the solution should be 1 grain to the ounce to begin with, and this may be gradually increased up to 8 grains to

the ounce if the patient can tolerate it. Albargin contains 13·4 per cent. of silver and can be used in strengths of 5 to 20 grains to the ounce. Argyrol contains 20 per cent. of silver and can be used in very strong solutions, up to 25 per cent. in some cases, but it is unfortunately very expensive.

(ii) *Astringents.*—These include zinc and copper sulphate, sulphocarbolate of zinc, resorcin, alum and a host of others. Before the pathology of chronic gonorrhoea (gleet) was known, the astringents enjoyed a great reputation, and many ingenious combinations were retailed by drug vendors as infallible cures for gleet. Since we now know that the gleety discharge depends in most cases on the presence of gonococci in the mucous membrane, astringents have been largely abandoned. When gonococci can no longer be found and a mucoid discharge persists, the effect of the astringents may be tried for a few days, as they are not likely to do any harm, and if they have the effect of diminishing or stopping the discharge, even temporarily, the patient will be pleased.

(3) Irrigations.—The object aimed at in irrigating the urethra is to wash the surface of the mucous membrane thoroughly by allowing a large quantity of fluid containing some mild antiseptic or astringent to flow over the surface, and in so doing to carry away any gonococci lying free, as well as those contained within pus cells, and toxin. Irrigations are merely to be used for the purpose of cleansing the surface of the inflamed mucous membrane in much the same way as we wash out an abscess cavity. No attempt should be made to destroy gonococci by means of irrigations, and strong solutions should never be employed. At the same time an irrigation acts as a mechanical massage to the mucous membrane and encourages a serous exudation which helps to bring the gonococci from the deeper layers up to the surface; the increased exudation probably also brings a greater supply of anti-bodies into contact with the gonococci and so tends to destroy them more rapidly. Some authorities think that this exudation instead of hastening the process of cure merely affords the germs a better food supply

and so tends to retard cure. Irrigations are of most benefit in the acute stage, when there is a copious discharge and many free gonococci lying in the urethra. In the chronic stage when there is only a scanty discharge, irrigations are of little use.

Some writers object to the employment of irrigations during the acute stage on the ground that they tend to give rise to complications, especially epididymitis. In a series of 896 cases treated by one of us (C. E. P.), 43, or 4·8 per cent., developed epididymitis while being treated by irrigations. The cases were not in any way selected and although we have no statistics to show the percentage of men who develop this complication when treated by other methods we feel sure that it would have been quite as high, if not indeed higher.

Apparatus.—A douche glass or can, rubber tubing with spring clip and nozzle, two macintosh aprons, rubber gloves and a slop bucket are required. The douche glass or can should have a capacity of at least one quart. When a number of men have to be treated

it saves time if the can has a capacity of a gallon ; larger than this is not suitable as in winter the fluid cools too quickly. A glass jar has the advantage that the operator can see the amount of fluid which he uses, so that when irrigating the posterior urethra he knows that the fluid is actually running into the bladder. With a can made of opaque material the operator does not know whether the fluid is running into the urethra or is merely pressing against an unrelaxed sphincter.

The rubber tubing should be about 7 feet in length to allow of some play between the can and the patient's penis. The spring clip is necessary in order to keep the stream shut off till it is required : when once the irrigation is begun the rate of flow can easily be regulated by pinching the tube.

The nozzle may be a simple glass tube with a blunt cone-shaped end or a double channelled one may be used.

The latter saves a great deal of time when irrigating the anterior urethra. The objection is however made that the fluid runs into

the urethra till it is full, after which the fluid merely enters the urethra by one opening and immediately leaves it by the other without having circulated round the urethra at all. To obviate this taking place a short catheter may be used in place of the nozzle and passed about half-way into the urethra; there are however considerable objections to passing an instrument into an acutely inflamed urethra. The other way is to use a blunt nozzle and apply this to the meatus: when the urethra is filled the nozzle is withdrawn sufficiently to allow the fluid to escape and the urethra is then filled again. The two macintosh aprons are required, one for the surgeon and the other for the patient. Both should be of full length in order to protect the clothes from stains; that to be worn by the patient should have a hole in the middle, through which the penis is pulled, and the sheet should be slightly depressed between the patient's thighs so as to form a drain along which the escaping fluid will flow into the slop bucket, which is placed between the patient's knees.

TECHNIQUE.—The douche can is filled with the

selected solution and raised by means of a pulley or hung on a nail in the wall at a height of 2 to 3 feet above the penis, if the anterior urethra only is to be irrigated, and not more than 5 feet for the posterior urethra. Greater heights are rarely necessary and may cause rupture of the compressor urethrae. The patient is now seated in an ordinary chair or on a stool of the usual height; he must be made to sit near the front edge so that his penis can be easily pulled out; if he sits well back, and especially if the chair is low, the penis seems to sink into a depression and it is difficult to pull it out sufficiently to permit of the necessary manipulations being carried out. The macintosh is next adjusted on the patient, taking care that the hole for the penis is not too large, as in that case the solution may run down inside the sheet and leave a nasty stain on the clothing. The operator, if he has not already done so, then puts on his own macintosh and if he is at all nervous about any pus reaching his eyes he should wear a pair of goggles. Rubber gloves are a luxury, but they protect the hands from unsightly staining. Rubbing grease on the

hands will also protect the skin but, as it makes the fingers slippery, it somewhat interferes with the surgeon's comfort during the subsequent manipulations.

The clip is next opened and some of the solution allowed to run out to test its temperature; if satisfactory the operator takes hold of the patient's penis and turns back the foreskin, at the same time directing a stream of the solution on to the glans and thoroughly washing this and the sulcus under the corona. The nozzle is then applied to the meatus and the solution allowed to flow gently into the urethra. The force of the stream can be regulated by pinching the rubber tubing between the forefinger and thumb of the right hand while the left one holds the penis. When a patient is receiving an irrigation for the first time he is usually a little nervous and it is wise only to allow a very gentle stream at first till he gains confidence. If using a simple nozzle, and the anterior urethra alone is to be irrigated, the nozzle must be withdrawn as soon as the fingers of the left hand feel that the urethra is distended or the patient complains of

any sensation of fullness. When the double channel nozzle is employed it need not be withdrawn till the irrigation has been completed. As a general rule we think that one pint of fluid is sufficient to wash out the anterior urethra, although some writers recommend much larger quantities.

As long as the outflow is acting the fluid does not, except in very rare cases, reach the posterior urethra. When it is desired to irrigate the posterior urethra the outflow tube is closed, or if a simple nozzle is being used it is held in position and the patient is told to try to pass water. This usually relaxes the sphincter and allows the fluid to run into the bladder. Some men are nervous, and when told to try to pass water the sphincter contracts spasmodically and obstinately refuses to relax. In such cases a little patience and talking to the man on some indifferent subject will often lead to the contraction suddenly ceasing. If this is not successful the height of the can may be increased to five feet, In very obstinate cases the injection of a few drops of a 2 per cent. solution of cocaine

will anaesthetize the mucous membrane and lead to relaxation of the sphincter. The solution should be permitted to run into the bladder till the patient complains of a sensation of fullness when it should be cut off. He should be told to retain the fluid as long as he comfortably can, but at least a quarter of an hour if possible, as this gives the medicament some chance of acting on the mucous membrane and any gonococci which happen to be on or near the surface of the bladder and posterior urethra.

When dealing with a number of men a supply of nozzles should be at hand, a clean one being used for each man, and the used one immediately disinfected either by boiling or in a strong antiseptic solution and then washed in sterile salt or boric acid solution.

Drugs.—The drugs most commonly employed for irrigations of the urethra are potassium permanganate, silver nitrate, albargin and zinc sulphate.

Janet employed the permanganate, and although we know that its bactericidal properties are feeble yet it certainly seems to yield

satisfactory results in this form of treatment. It is especially suited to the acute stage of gonorrhoea as it does not cause any irritation and is mildly astringent. At first it should be employed at a strength of 1 grain to the pint and later on increased to 2½ grains to the pint. The simplest plan is to have a stock solution containing 1 grain of potassium permanganate in each ounce of solution; the required number of grains can be taken by simply pouring into the douche can filled with warm water the same number of ounces of stock solution and stirring the mixture. In all irrigations the temperature of the fluid should be as near that of the body as possible. A point worth remembering is that the weak solutions are usually just as effective as strong ones and are less likely to cause irritation.

The next most useful drug is silver nitrate. This should be used in a strength of 1 grain to the pint at first, later on it may be increased to 2 grains. Silver nitrate is most effective in the subacute and chronic stages. It seems to have a slightly stimulating and tonic effect on the mucous membrane and to hasten the disappear-

ance of the fine haze so often seen in the first morning urine.

Albargin, 2½ to 5 grains to the pint has much the same action as silver nitrate ; it is much more expensive.

In some chronic cases, in which the presence of mucus in the early morning urine persists for a time, irrigations with zinc sulphate 5 grains to the pint sometimes produce a marked improvement.

Many other drugs have been used, and provided the water is not forgotten, and not too much of any drug added to it, the results may be equally good.

As to the number of times the irrigation should be given daily, opinions differ. In the acute stage we favour two irrigations a day ; one in the morning and one in the evening, with some mild injection, e.g. protargol 1 grain to the ounce at night just before going to bed. Others recommend three irrigations a day, and if there is much discharge this practice would seem to be sound, as the purpose of the irrigation is to wash the urethra clean.

What are the advantages of irrigations over injections?

In the first place the patient gets the treatment as it is administered to him and not left to his own inclination to carry out or not as he pleases. Secondly the urethra is thoroughly washed out and all inflammatory products and free gonococci are removed. Thirdly the acute stage is very much reduced in duration.

The disadvantages are that a special room of some sort is required and also a small amount of apparatus; the surgeon's hands are liable to get badly stained; it is messy, and nervous patients may be frightened by the formidable appearance of the apparatus.

(4) Bougies.—Many attempts have been made to treat gonorrhoea by the introduction of medicated bougies. The earlier forms consisted of iodoform and similar antiseptic substances made into a bougie with oil of theobroma. This medicated bougie was introduced into the urethra and left to melt there with the idea that the drug would thus be deposited in the urethra and continue to act for some considerable time.

These trials ended in failure, largely because the fatty base prevented the drug from coming into contact with the mucous membrane and partly also because the drugs selected had only a low bactericidal power for gonococci.

More recently Karo has described a hollow bougie containing one of the newer silver salts in an emulsion and has claimed considerable success from the use of these. The introduction of any hard or firm body into an inflamed urethra does not seem to be a sound practice. Leistikow uses bougies the basis of which is Unna's paste mass and consists of starch, sugar, dextrin and a little glycerine and is therefore soluble in watery secretions. Any desired drug is incorporated in this mass which is then rolled into bougies 10 to 18 cm. in length and 2 to 4 mm. in thickness. Before being used they are dipped into hot water which makes the surface smooth and slippery.

(5) Symbiosis.—In Germany attempts have been made to get rid of the gonococci by introducing yeast pellets into the urethra. Sterilized cultures of B. pyocyaneus have also been tried,

but the results in both cases have been decidedly unfavourable.

(6) MECHANICAL MEANS.—When the disease has reached the chronic stage little can be effected by injections or irrigations alone and one of the following means may have to be employed.

(*a*) *Bougies.*—For many years it has been known that the passage of a solid metal bougie frequently resulted in the diminution of the gleety discharge and the treatment is still in common use. How it acts is not quite clear. It used to be thought that the bougie stretched the urethra and opened out all the folds of the mucous membrane, but as the meatus is the narrowest part of the urethra any instrument which passes through it cannot fully distend the urethra. The passage of the bougie may have the effect of causing a mild hyperaemia of the mucous membrane, or of dislodging secretion blocking the mouths of Littré's glands, or of stimulating the surface of a sluggish ulcer.

(*b*) *Dilators.*—These instruments when closed can be passed through the meatus into the urethra, and when in position the blades can be

separated by a screw mechanism, the extent being shown on a dial. The blades should be screwed open as far as the patient can tolerate and kept in this position for some five minutes. The degree of dilatation as shown by the dial should be recorded and at the next application it will probably be found that the patient can tolerate a slightly greater extension.

When the blades are fully opened up the mucous membrane is tightly stretched as also are any soft infiltrations which may be present, while the contents of any inflamed follicles are expressed into the urethra ; these must be removed at once by means of an irrigation. Kollmann's dilator is so constructed that the irrigation may be employed while the instrument is in position.

A curved form of dilator is sometimes used for the posterior urethra. The advantage is doubtful, as much of the dilating force must be used up in overcoming the resistance of the compressor urethrae. The prostatic urethra being surrounded by the somewhat unyielding prostate gland cannot be stretched like the anterior urethra. The posterior urethra is also much more sensitive

than the anterior and does not therefore lend itself to forcible dilatation.

(*c*) *Instillations.*—Before the general adoption of endoscopic medication instillations by Guyon's and Ultzmann's syringes were freely used in the treatment of small urethral ulcers or inflamed patches. The diseased spot was first located by means of a bougie, the syringe was then introduced, the eye of the cannula being brought as near the diseased spot as possible, and a few drops of a strong solution of nitrate of silver were then expressed on to the urethral surface.

(*d*) *Prostatic Massage.*—When gonococci have invaded the prostatic ducts an attempt may be made to expel them by massaging the prostate. This is carried out by inserting the finger, protected by a finger-stall, into the rectum and massaging the prostate; an electric masseur may be employed in place of the finger. The massage should be employed for one to two minutes at a time and repeated every second or third day. The massage has the effect of expressing some of the prostatic secretion into the urethra and of

relaxing the compressor urethrae muscle as the secretion appears at the meatus. In its passage through the ducts the secretion carries some gonococci and inflammatory exudation with it and thus no doubt the massage does help to reduce the severity of the infection; but after all it is only the gonococci lying free within or on the surface of the ducts which are removed, not those occupying the epithelial lining of the ducts. The urethra must be irrigated at once in order to wash away the gonococci which have been deposited in the urethra by the massage. The effect of massaging the prostate may be enhanced by giving an injection of gonococcal vaccine a few days previously.

Schindler has shown that mechanical irritation of the prostate sets up reverse currents in the vas deferens which would be very likely to carry gonococci to the epididymis. These currents can be prevented by the action of atropine. An hour before massaging the prostate a suppository containing 2 mgm. of atropine should be inserted into the rectum.

Choice of Method.—The particular line of

treatment adopted must depend mainly on the stage of the disease when the patient is first seen. If seen at a very early stage of the disease before the symptoms have become fully developed, i.e. before the discharge has assumed a purulent character, it is quite worth while trying the so-called "abortive" treatment, as, even if this fails to cut short the disease the patient is no worse off.

The "abortive" treatment is based on the idea of destroying the gonococci before they have penetrated the epithelium and is carried out by injecting strong bactericidal solutions. As these generally cause acute pain it is well to begin by injecting some local analgesic, e.g. a 2 per cent. solution of cocaine. The best results are obtained by using one of the silver salts, e.g. nitrate of silver 2 per cent. solution, protargol 2½ per cent. to 5 per cent. solution, or argyrol 10 per cent. to 25 per cent. solution. The urethra should first be washed out with non-irritating fluid; the selected drug is then injected and held in the urethra for a quarter of an hour. The procedure should be repeated once or twice at intervals of a

few hours. A mild injection, say, weak potassium permanganate solution should be used to wash away the resultant discharge. It is unfortunately only in rare cases that the treatment is worth trying as in the stage at which patients usually present themselves the disease has progressed too far to permit of a successful result being obtained.

In the ordinary acute case, and this is the condition in which patients usually present themselves for treatment, the surgeon's choice of method must depend on the facilities which he has for carrying out treatment and the patient's circumstances. We believe that the irrigation treatment considerably lessens the duration of this stage and would always employ it for patients in hospital and for those who could attend to have it carried out. At the same time the injection treatment with one of the newer silver salts yields satisfactory results provided the patient follows the instructions given him. In any case some form of urethral medication should be employed.

In the subacute and chronic stages injections

are probably as effective as any method of treatment. When these stages have been reached urethral medication becomes of secondary importance to the maintenance of the patient's general health. To accomplish this end the patient must be well fed and kept out of doors as much as possible: if we insist on keeping him in bed on a milk diet, at this stage of the disease, we are doing our very best to prolong the duration of symptoms indefinitely.

The treatment of each stage may be tersely summed up as follows:

(1) *The very early case.*

Keep quiet during the day.

Diet: No restrictions except alcohol and spices.

Injections: Protargol grs. 10 to 16 to the ounce; three injections to be given at each sitting, each to be retained for five minutes; repeat this twice during the day. On the next two or three days use a weak potassium permanganate injection thrice daily.

No internal treatment.

(2) *The extremely acute case.*

Put the patient to bed. If available, employ a continuous hot bath for several hours daily.

Diet: Milk and barley water only.

Internally: Saline purges, alkalies, hyoscyamus, morphia suppositories, bromide of potassium, atropine suppositories.

No urethral medication.

(3) *The acute stage.*

Allow the patient to sit up during the day with a very limited amount of gentle walking exercise.

Diet: Milk, barley water, soda water, weak tea or coffee, eggs, fresh white vegetables, butter and bread.

Internally: Saline purges, alkalies, hyoscyamus.

Irrigations with potassium permanganate gr. 1 to the pint, or injections of protargol beginning with gr. 1 to the ounce.

(4) *The subacute stage.*

Allow the patient up all day with gentle exercise.

Diet: No alcohol or spices, otherwise no restrictions.

Internally, balsams (if not objected to by the patient).

Irrigations with potassium permanganate grs. 2 to the pint, twice daily; or nitrate of silver grs. 2 to the pint, or albargin grs. 2½ to 5 to the pint.

Or injections, protargol grs. 4 to 8 to the ounce.

(5) *The chronic stage.*

Allow the patient up all day, with any form of exercise except cycling or riding.

Diet: No alcohol or spices, otherwise a liberal diet.

Internally tonics, cod liver oil, sanatogen, iron and arsenic.

Irrigations, nitrate of silver grs. 2 to the pint, or albargin grs. 5 to the pint, or zinc sulphate grs. 5 to the pint, once daily. Or, injections of zinc sulphate grs. 2 to the ounce, or protargol grs. 8 to the ounce, once a day.

Prostatic massage, dilatation, or endoscopic examination as indicated.

Duration of the Attack.—We must honestly confess that at present we know very little about the average duration of an attack of gonorrhoea, and when we speak of the disease lasting on an

average six weeks we only mean that in the ordinary case we may hope for an apparent cure after six weeks' treatment.

The time of treatment varies very much with different individuals and depends on: (1) The man's own resisting powers or natural immunity; (2) The treatment adopted and the depth to which the gonococci have penetrated before the treatment was begun, and (3) The standard of cure adopted by the surgeon. The last is really the most important factor, for if the surgeon is easily satisfied that a cure has been effected, the time of treatment may be very much cut down and some brilliant results shown irrespective of the treatment adopted, provided the cases are not further followed up and the percentage of relapses added as an appendix to the statistics. The determination of cure is really most difficult, and at present we are obliged to rely on more or less empirical rules.

We have used the following plan: When the urine has become clear and the threads, if present, are not found to contain gonococci the treatment is reduced; if no return of symptoms takes

place it is entirely omitted at the end of about five days. During the next three days no further treatment is given but the urine is carefully watched for signs of a return of the inflammation. If the condition of the urine remains satisfactory the man is then given a pint of beer and four ounces of mixed pickles daily for another five days. If this fails to induce any signs of a relapse the man is dismissed with strict injunctions not to indulge in any alcohol or sexual intercourse. When these instructions are obeyed and the man is leading a healthy life it is unusual to find a relapse.

Schindler gives the following plan: When the urine becomes clear he stops the protargol and substitutes icthargan, 1 in 3,000, for it. Any gonococci left in the urethra begin to grow again and show signs of their presence in three to four days. If nothing happens the icthargan is stopped and no treatment is given for three days; the patient is then examined and, if apparently well, icthargan is again ordered for three days after which all treatment is omitted for two days. Three injections of silver nitrate,

1 in 1,000 are then given and the discharge is examined next day for gonococci. If this proves negative Schindler concludes that the patient is cured.

The principle in both cases is the same, viz. to go on with the treatment till the patient is apparently cured and then to administer some form of treatment or diet, designed to cause urethral irritation, in order to stir up any quiescent gonococci so that they may show themselves in the discharge. Schindler's plan is more scientific but ours is more popular, as any man would prefer to drink a pint of beer daily rather than have even a mild return of urethral scalding to satisfy his doctor's curiosity. In either case the verdict of "cured" should read "apparently cured," as gonococci may still be present in a quiescent condition in spite of our efforts to rouse them to fresh activity.

Relapses.—It is extremely difficult to get any reliable statistics as to the frequency of relapses, i.e. the number of cases which are apparently cured but in reality are not so. Much depends on the care taken in the first place to

ensure that a cure was effected before dismissing the man. Again, patients who return shortly after being "cured" of a gonorrhoea usually deny having exposed themselves to a fresh infection, and of those who own to having done so it is quite open to question whether the man did really contract a fresh gonorrhoea, or merely that the act of sexual connexion stirred some latent focus of gonococci into renewed activity.

In a series of 734 cases, treated by one of us, in which every endeavour was made honestly to record all genuine relapses, thirty-four such were noted: this would give a percentage of 4·6, but we must admit that in view of the difficulties involved in distinguishing a relapse from a fresh infection this figure may be quite wrong.

CHAPTER VI

COMPLICATIONS IN THE MALE

In this chapter it is only intended to discuss the complications which are caused by the extension of the gonococcal infection from the male urethra to adjacent parts, leaving those conditions which are due to a gonococcal metastasis and therefore common to both male and female, to a later chapter.

The conditions to be considered at present are: oedema of the prepuce; warts; oedema of the penis; lymphangitis of the penis; haemorrhage from the urethra; infections of Littré's glands and of paraurethral ducts; penile abscess; infection of Cowper's glands; prostatitis; epididymitis; cystitis; pyelitis; perinephritic abscess; lymphadenitis of the inguinal glands; soft and hard infiltrations, and stricture of the urethra.

Oedema of the prepuce or penis occurs during the acute stage and is probably caused by the gonococci gaining entrance into the lymphatics and causing a temporary lymph stasis. The condition usually merely amounts to a temporary discomfort lasting for a few hours; in rare cases it may lead to the formation of superficial abscesses. The patient should be kept in bed with the penis in an elevated position till the oedema has passed off. The surface of the glans penis and prepuce should be kept as free from accumulations of discharge as possible and hot fomentations applied to the penis.

In Germany warts are regarded as almost diagnostic of gonorrhoea; they are probably due to the irritation caused by decomposing discharge. Their treatment is frequently very troublesome. Thorough cleanliness of the parts should if possible be obtained by soaking the penis in an antiseptic solution. An attempt to get rid of the growths must then be made. For this purpose astringent drugs, e.g. solid sulphate of copper or caustics like pure carbolic acid, nitric acid, etc., may be applied to the surface

of the growths. These applications are however usually ineffective and are extremely likely to get on to the surface of the glans and cause severe excoriation of the part. The actual cautery or a scalpel may be used to remove the warts but this is never an easy operation, as they are very sensitive and bleed freely when the surface is broken. Very large masses have been successfully removed by repeated exposures to "X" rays.

Slight haemorrhage from a congested vessel in the urethra may take place during the acute stage of gonorrhoea. If the patient is kept at rest the oozing will generally cease in a few hours without any further treatment; if not an ice-bag may be applied or an astringent injection given.

Littré's glands are probably infected in every case of gonorrhoea and the infected glands are one of the principal causes of gleet. The condition referred to here is that in which the mouth of the duct becomes blocked and the gland itself distended with inflammatory exudation. This exudation may at intervals force open

the duct and discharge pus and gonococci into the urethra, or the gland may become distended with muco-purulent matter and form a minute cyst, or again the contents may burrow outwards and lead to the formation of a penile abscess. If this happens it should be treated in the usual surgical way when it will speedily heal up. A cystic condition of the gland can only be detected by means of the endoscope. An attempt should be made to slit up the cyst or destroy it by means of the electric cautery. In some cases by passing an olive-headed bougie into the urethra, till its shoulder rests on the infected gland, its contents may be emptied by massaging the penis on the bougie. As the glands are very small and are situated in the urethra at varying distances from the meatus, any form of treatment is extremely difficult to carry out.

Paraurethral ducts are fortunately of somewhat rare occurrence as, owing to their length and very small lumen, if they become infected with gonococci, treatment is difficult and unsatisfactory. Medication is useless and the duct

must be destroyed. If it happens to be a short one it may be possible to dissect it out, if not an attempt should be made to destroy it by electrolysis or by injecting caustic fluids through a hypodermic syringe.

Chordee.—This highly unpleasant complication, which formerly used to be regarded as quite an ordinary manifestation of the disease, is supposed to be due to contractions of the longitudinal muscular layer of the urethra. In some cases it appears to be due to inflammatory deposits in the cavernous tissue preventing the blood spaces from becoming fully filled on one side of the penis and so producing a bent and very painful erection. Much may be done to prevent the occurrence of chordee by administering sedatives to allay the irritability of the erector penis. Potassium bromide in full doses has a good reputation but we have found it very disappointing.

Suppositories containing a full dose of morphia are much more effective. Schindler recommends a suppository containing 2 to 3 mgm. of atropine, to be used at bed time. The predispos-

ing factors should also be attended to, viz. sleeping in a soft warm bed with too many bed clothes, reading exciting French novels, constipation.

When chordee is actually present the penis should be immersed in cold water, iced for preference, and a cold compress applied to the perineum.

Inflammation of Cowper's Glands.—In probably every attack of gonorrhoea the ducts of Cowper's glands become more or less affected, but it is rather exceptional for the condition to be sufficiently marked to be recognized; in these cases it may go on to the formation of an abscess. The symptoms are dull throbbing pain in the perineum accentuated by the act of micturition. If an abscess forms it may burst into the urethra or point externally in the perineum. In the early stage fomentations to the perineum may give some relief; if pus forms the abscess must be incised and treated in the usual way.

Prostatitis.—This probably occurs to a slight extent in every case in which the posterior urethra is invaded by gonococci, but it is not often

that the condition advances far enough to be recognized as a distinct inflammation of the gland. The German writers classify prostatitis as catarrhal, follicular or parenchymatous, and lay down distinguishing symptoms for each of the varieties. This seems to us to be somewhat unnecessary.

The symptoms are pain in the perineum, which may be dull or acute and is much aggravated by passing a motion or on micturition. Examination per rectum reveals the swollen and very tender condition of the prostate. If pus has formed there is usually a soft spot and fluctuation may even be detected. Treatment: If the whole gland is inflamed and tender, but no definite softening can be made out, an injection of gonococcal vaccine is indicated, and in one of our cases this acted like magic. At the same time warm sitz baths may be tried, as also fomentations or leeches to the perineum. Schindler strongly recommends suppositories containing full doses of atropine together with iodide of potassium and expressly states that all mechanical irritation, e.g. repeated examina-

tions, should be avoided. If pus has formed it may be evacuated by way of the rectum or the perineum; much has been written as to the best route to adopt, but it seems only sensible to puncture the abscess at the spot at which it can most easily be reached.

Soft and Hard Infiltrations.—Soft infiltrations are plastic exudations into the submucous connective tissue of the urethra; of themselves they cause no symptoms unless perhaps persistent gleety discharge. If left alone the exudation is in time converted into fibrous tissue and the infiltration is called a hard one. This in turn contracts and leads to the formation of a stricture.

Soft infiltrations can only be detected by the endoscope or by the olivary headed bougie. The tapering shape of the point allows this instrument to be passed along the urethra through a soft infiltration; it is then withdrawn in short sharp jerks; when the shoulder meets a soft infiltration a sense of resistance is felt.

The treatment consists in mechanical dilatation. Solid metal bougies are useless for this

purpose as the meatus is the narrowest part of the urethra and any instrument which passes through the meatus cannot possibly dilate the canal beyond. One of the screw pattern dilators must be used for this purpose. Kollmann's is quite satisfactory. Strict aseptic precautions must be observed. The best lubricant is one of the aseptic jellies sold in tubes; these jellies are soluble in water and therefore do not interfere with the action of any drug which may be subsequently employed, as vaseline or oil may do. The instrument must be passed for its full length into the urethra and the blades then opened up till the patient complains of commencing pain. The instrument should be kept in position for about five minutes and meanwhile an irrigation of potassium permanganate run through. This can be done with Kollmann's irrigating dilator, but if this is not available the irrigation must follow immediately afterwards so as to wash away any expressed secretion. The dilatation should be repeated every second day, and an attempt made to dilate the urethra a little more each day. A hard infiltration should

be treated in much the same way. Should a stricture form it must be treated as laid down in works on surgery.

Epididymitis.—This, which is one of the commonest and best known complications of a gonococcal infection of the male urethra, usually affects only one testis but may attack both at the same time. It is not possible to state what the incidence of epididymitis is. Among 896 cases, treated by one of us, 74, or roughly 8 per cent., were admitted with this complication, while in 43 or 4·8 per cent., it developed subsequent to admission. Schindler thinks that the infection is carried along the vas deferens by backward currents, and he strongly advocates the use of atropine in all cases in order to stop the contractions of the muscle in the walls of the vas; he has shown by experiments on animals that irritation of the prostate and colliculus seminalis sets up these backward currents and that atropine inhibits them. The earliest symptom is acute pain in the groin shooting down to the testis. In a few hours the epididymis becomes swollen and exquisitely

tender. At the same time there may be some pyrexia and the patient feels out of sorts. The vas becomes swollen, and if the infection has lasted for a few days the vas feels hard like a piece of iron piping.

The swelling may clear up in a week to a fortnight. Sometimes it persists for a much longer time, leaving the epididymis firm and little sensitive; later on the plastic exudation becomes organized into fibrous tissue and the epididymis shrinks, or fibrous nodules may persist in the cauda. In these cases the testis has almost certainly lost its function.

TREATMENT.—If the inflammation is acute the patient should be sent to bed. Owing to the risk of the testis being permanently damaged energetic treatment should be begun at once, by injecting gonococcal vaccine; this may be repeated if necessary. In some cases, such as the two reported below, the results are striking, in others disappointing, but even if it fails the patient is no worse for it.

CASE 1. EPIDIDYMITIS.—Gunner H. Infection was stated to have taken place on February

24, 1909. He was admitted to hospital on March 10, 1909, with subacute gonorrhoea and epididymitis, his temperature being then 101.4°F. The usual treatment was applied without any beneficial result. On March 12, 1909, he received an injection containing 250 million gonococci (Parke, Davis & Co.). The same evening his temperature was 102°F. but after this it fell steadily and was normal on the third day after the injection; the epididymitis cleared up at the same time. All the other signs of the disease rapidly disappeared and he was discharged from hospital, apparently cured, seventeen days after receiving the injection.

Case 2. Epididymitis.—Sapper B. Second attack of gonorrhoea, date of infection not definitely known. He was admitted to hospital on February 13, 1909, with acute gonorrhoea, epididymitis and pyrexia. The usual treatment was tried but without effecting any apparent benefit. On February 15, 1909, he was given an injection containing 250 million gonococci (Parke, Davis and Co.). On the morning of the injection his temperature was 103·4 but after the injection

it fell rapidly, reaching normal on the third day. At the same time all his symptoms rapidly cleared up and he was discharged from hospital apparently cured on the fourteenth day after the injection.

The next measure to adopt is to support the testis so that it cannot drag on the vas; this affords great relief to the pain. While a patient is in bed the testis may be supported by placing a piece of carboard or other stiff material with a pad of cotton wool across his thighs and laying the testes on this. Unfortunately if the patient turns in his sleep his testes slip off and cause him considerable pain. A triangular bandage fastened round the body and folded so as to make a sling in which the testes rest, with a hole cut in the front fold for the penis to pass through, is a useful support. The old suspensory bandage is of some help but fails to keep the testes sufficiently immobilized. In mild cases when the man is allowed up the testes may be fairly well supported by gathering the lower portion of the scrotum into a fold and retaining it in this position by passing a strip of soft adhesive

plaster round it; this keeps the testes in the upper portion of the scrotum.

The most satisfactory form of support is Horand's which is used in Vienna. It consists of two triangular pieces of calico; these are sewn together and form a shallow pouch. A hole is cut for the penis to pass through. A long tape is sewn to each of the top corners and two tapes to the lower point. To apply it, the patient is told to lie down; the surgeon with one hand raises the patient's scrotum and testes as high as they will go on to the abdomen. The point of the bandage is then placed on the perineum just behind its junction with the scrotum, and the space between the bandage and the testes is filled in with cotton wool; the bandage is next brought up over the testes, the penis is passed through the hole made for it and the lower tapes are brought up round the back of the thighs and tied to the upper ones, which are fastened round the man's waist. Any space between the testes and the bandage is then packed with cotton wool so as to immobilize the testes completely.

Puncturing the tunica vaginalis to allow the inflammatory exudation to escape has been recommended: this practice often gives great relief in painful cases but may lead to damage to the tubules. Fomentations give some relief if there is much pain. Counter-irritants are useful in subacute cases. The drug selected should not be likely to blister as the scrotum quickly becomes excoriated and the resulting lesion may take a long time to heal up. Guaiacol 10 parts vaseline 100 parts, spread on lint and applied to the testis will often afford considerable relief. When the tenderness has subsided, the testis may be strapped over mercurial ointment. The local treatment is however merely to be looked on as an adjuvant to the injection of vaccine.

Adenitis.—Inflammation of the lymphatic glands of the groin is not an uncommon complication of gonorrhoea in the male. The inflammation is usually of the subacute variety, that is, the gland becomes swollen but remains fairly firm in consistence and the skin is not as a rule involved. Suppuration does not

usually occur, but if it does only a small portion of the gland suppurates, the remainder being boggy. After incision the wound heals fairly quickly and the adenitis clears up. Gonococci have been recovered from the contents of these glands on many occasions, but when suppuration occurs there is usually a mixed infection and other pyogenic germs are found.

In many cases of the so-called non-venereal bubo there is a history of an attack of gonorrhoea generally of a somewhat protracted nature. A probable explanation seems to be that some of the gonococci become encapsuled in the gland and lie there quiescent till some mechanical injury lowers the vitality of the gland and permits the gonococci to become virulent again.

Retention of urine may occur in consequence of a spasmodic contraction of the sphincter due to acute gonorrhoea. The usual treatment for this condition will generally suffice to relax the sphincter; if this fails the urethra should be anaesthetized and a catheter passed, but if possible this should be avoided.

Cystitis and Pyelitis.—Cystitis probably

occurs in every case in which the posterior urethra is attacked. The condition rarely receives and indeed does not as a rule merit any special attention. In this condition the balsams might reasonably be expected to be of some use as the products, being excreted in the urine, would be for some time in contact with the bladder walls.

When the gonococcal infection ascends the urethra and reaches the pelvis of the kidney the condition is much more serious. Usually only one kidney is affected and the process may be limited to the pelvis of the kidney or it may give rise to a perinephritic abscess. Gonococcal infection of the kidney gives rise to a great deal of constitutional disturbance with pyrexia and a dull aching pain in the loins.

The patient should be put to bed and kept at rest on a milk diet with plenty of fluid to drink. Gonococcal vaccine is indicated at once and should be repeated at intervals of a few days. Drugs have little effect on the condition. Some of the newer preparations of sandalwood oil, e.g. gonosan, which, it is claimed, do not contain the

irritating constituents of sandalwood oil, should be of service. One case under my own care did very well on urotropine, but whether the cure was due to the drug or the patient's own powers of recovery it is difficult to say. Irrigations of the pelvis of the kidney with 1 in 1,000 nitrate of silver have also been recommended but should only rarely be required. The prognosis is generally good.

CHAPTER VII

GONOCOCCAL INFECTIONS IN THE ADULT FEMALE

Path of Infection.—In practically every case in adults the infection is introduced during coitus and by a male who believes himself to be cured of the disease. The act of connexion stirs up the latent foci of gonococci in the male urethra, and if the act be prolonged or repeated within a few hours a certain number of gonococci are certain to be ejected along with the semen into the vagina or even directly into the cervix uteri. Infection might possibly be acquired by the vulva coming into contact with a drop of infected pus on the seat of a water closet, but even in the case of a female this must be of rare occurrence. An infected diaper or towel might also be the means of conveying the infection as the gonococci

retain their virulence as long as they remain moist.

Anatomy.—When discussing gonococcal infections in the female the anatomical points to be remembered are:—

(1) The cervix uteri leads into the body of the uterus and hence along the Fallopian tubes to the peritoneal cavity. Thus not only the peritoneum but the organs concerned in procreation are directly exposed to the invasion of the gonococcus. The cervix uteri is lined with cylindrical epithelium and has mucous glands running deeply into its substance; these afford the gonococci an unassailable stronghold.

(2) The vagina is lined with squamous epithelium and therefore does not offer such a favourable site for the growth of gonococci.

(3) The female urethra is short and has no important glands opening into it.

(4) The glands of Bartholin are somewhat deep seated and open into the labia majora through long ducts. If gonococci once effect a lodgment in these ducts it is extremely difficult to reach them by any form of external treatment.

Site of Infection.—The two principal centres of primary infection are the cervix uteri and the female urethra. It is difficult to say which is usually infected first, but the chances are that the gonococci first of all gain a foothold in the cervix and that the discharge trickling down into the vagina infects the urethra.

Symptoms.—The symptoms of gonorrhoea in the adult female vary greatly in different cases much more so than in males. In young adults suffering from a first acute attack there may be great pain about the vulva and vagina accentuated on micturition or passing a motion; there is usually a copious purulent discharge and the parts are swollen and inflamed. If the infection has ascended to the body of the uterus and tubes there is certain to be severe abdominal pain with pyrexia and considerable constitutional disturbance.

In many of the subacute cases almost the only symptom is a mucopurulent vaginal discharge. In chronic cases the signs of the disease may be so ill-defined that the patient believes herself to be in good health; inspection with the aid of a

speculum may only reveal a slight mucoid discharge from the cervix in which gonococci can be detected with difficulty or none may be found. The symptoms in fact, as in all gonococcal infections, are those of inflammation varying with the extent and severity of the process.

Diagnosis.—This resolves itself into determining that inflammation exists and that it is due to gonococci. In the purulent discharge of acute or subacute cases there is usually no difficulty in finding gonococci, and although other germs may be present the gonococci may safely be held to be the culprits. In the chronic case gonococci may be very scarce in the discharge and their presence may easily be overlooked. Culture tests may be tried, but as the gonococcus is not by any means an easy germ to cultivate a negative result does not yield a definite conclusion. The best time to search for gonococci is at the end of menstruation when the gonococci may be found adhering to the shreds of mucous membrane passed at this time.

Prognosis.—Gonorrhoea in the female is, owing to the anatomical relations of the site of

primary infection to the important pelvic organs, a much more serious disease than in the male. The danger to the patient's life is not very great, but if once the uterus and appendages become infected the disease is likely to persist for years, possibly up till the change of life occurs. During this time the patient will almost certainly be barren, will probably suffer much pain and possibly require surgical interference for the removal of some collection of pus due to the presence of gonococci. A less severe infection may cause a chronic endometritis leading to the expulsion of the fertilized ovum from the uterus; plastic adhesions may prevent any ovum from reaching the uterus: in the first case the woman remains barren, while in the second the result may be a tubal pregnancy. About one-third of childless marriages are attributed to the presence of gonococci in the female.

Even when the infection remains localized to the cervix and urethra the gonococci tend to persist for a long time and in the present state of our knowledge it is quite impossible to say when the parts are free from gonococci. During

this time there is always the risk of infecting her husband or her child's eyes, should she have one.

The prophylaxis has been discussed in the introductory chapter.

Treatment.—Owing to the great extent of mucous membrane which may be invaded the treatment of gonococcal infections in the female is even more unsatisfactory than in the male. As in the male the success or otherwise of the treatment adopted depends mainly on the depth to which the gonococci have penetrated the mucous membrane before treatment is begun.

Treatment may conveniently be discussed under the headings: (1) Local, (2) Internal, (3) Vaccines, sera and symbiosis.

(1) THE LOCAL TREATMENT aims at destroying or removing the gonococci and their toxin. In acute or subacute cases with much discharge douches should be employed; after the douche a gonococcicidal agent should be applied to the surface of the mucous membrane.

Copious hot douches, up to twenty or thirty pints at a temperature of 110° F., not only

wash away the gonococci and toxin, but by causing an active hyperdemia of the parts greatly accelerate the process of cure. As their action is mainly a mechanical one, the solutions selected should be weak and non-irritating but should be employed once or twice in the day according to the amount of discharge.

The actual drug employed is of minor importance; potassium permanganate 2 grains to the pint is cheap and fulfils the object aimed at; it has also a slightly astringent and soothing effect on the mucous membrane.

When the inflammation is less acute, stronger local applications are indicated. The most effective drug is nitrate of silver or one of the newer organic compounds of silver. In hospital practice the patient may be placed on a table in the dorsal position when about an ounce of the solution can be poured into the vagina and allowed to come into contact with every portion of the walls. If this position is objected to, the patient may be placed in the lateral position and the solution be applied by means of a moistened swab or brush through a speculum. To

reach the mucous membrane of the cervix or urethra some cotton wool should be tightly wrapped round a stylet or long probe, moistened with the solution and then passed into the canal and left there for a minute or so. The urethra may also be injected by means of a hypodermic syringe fitted with a blunt cannula.

The following solutions are suitable, the weaker ones being used when the inflammation is acute and the parts sensitive. Nitrate of silver ½ to 2 per cent., protargol ½ to 2 per cent., albargin 5 to 10 per cent., argyrol 5 to 20 per cent. Icthyol and resorcin are also favourite applications among continental practitioners. Strong solutions are not necessary and are more likely to do harm by causing irritation of the mucous membrane than to do good by killing the gonococci.

If there is much discharge a pledget of cotton wool saturated with a 2 per cent. solution of peroxide of hydrogen may be left in the vagina and changed at more or less frequent intervals. A piece of lint spread with some non-irritating ointment such as zinc ointment and vaseline

equal parts should be placed between the vulvae to keep them apart. A pad of antiseptic absorbent gauze should be worn outside the vulva in order to take up the discharge and prevent it from reaching the rectum.

Hot hip baths often afford a certain amount of comfort to the patient but can hardly be expected to influence the disease.

INTERNAL TREATMENT.—The balsams have not attained to the same popularity as in the case of the male, and as the female urethra is very short there does not seem to be sufficient reason for insisting on their use. Sedatives, e.g. bromides, opium, belladonna may be of use in the acute cases. Atropine, as recommended by Schindler to stop the contractions of the smooth muscle tissue which enters so largely into the composition of the female pelvic organs, certainly holds out some hope of checking the upward spread of the infection, but all internal treatment can only exert a mild influence on the course of the disease.

VACCINE TREATMENT.—This is the only form of treatment which holds out any prospect of really

effecting a cure when once the infection has spread beyond the parts which can be reached from without. Friedländer (*Berlin. Klin. Wochenschr.* No. 36 of 1910) using Reiter's vaccine reported that in most cases all symptoms had disappeared in four weeks.

Symbiosis.—Watson (*Brit. Med. Journal*, January 22, 1910) reported very good results from the use of lactic acid bacilli. These were grown in milk and the filtered whey was introduced into the previously cleansed vagina. The secretion sometimes increased for a few days, then became thin and non-purulent. In most cases the secretion became normal in a few days, if not the treatment was repeated once a week. The efficacy of the treatment depends on the antagonism between the lactic acid bacilli and the gonococci.

The Sequelae Special to Gonococcal Infection in the Adult Female.—The sequelae, or as one should almost call them, the complications of female gonorrhoea are due to extensions of the infection upwards to the pelvic organs or downwards towards the perineum.

The upward extensions probably take place more or less in almost every case, but it is only when the inflammation is sufficiently severe to require special treatment that they are noticed.

The body of the uterus may be infected leading to an endometritis; the infection may spread to the tubes setting up a salpingitis or even extend to the peritoneum and cause a peritonitis. The signs and symptoms of these complications belong to gynaecology and we may merely remark that in common with all gonococcal infections the signs are those of inflammation of a varying degree.

As to the frequency of their occurrence considerable differences of opinion exist. Pankow at the '82 *Versammlung deutscher Naturforscher und Aertze* stated that in his practice 43 per cent. of all inflammatory conditions of the uterine appendages were due to gonococcal infection. Noeggerath put the number much higher, but this has not been confirmed by subsequent observers. Ivens (*Brit. Med. Journ.* June 19, 1909) found that 24 per cent. of his gynaecological in-patients were suffering from the

effects of a gonococcal infection. Other estimations vary from 4·5 per cent. to 28 per cent.

The results of a gonococcal infection of the uterus and appendages have been discussed under the prognosis of gonorrhoea in the female and need not be repeated here.

The treatment of a gonococcal infection of the uterus and its appendages is very unsatisfactory. With the exception of the body of the uterus, and then only after dilatation of the cervix, the parts cannot be reached from without. Curetting of the uterus was formerly practised but is not generally advised now. The usual hot hip bath and counter-irritant treatment may be employed, as it will comfort the patient, but is not likely to have much effect on the progress of the disease. The one and only effective remedy at present is the bold use of gonococcal vaccine. The patient must of course be kept in bed during the acute stage.

The downward extensions may lead to infection of Bartholin's glands and the rectum.

Bartholin's glands are somewhat deep-seated and have rather long ducts. In a series of 591

cases of female gonorrhoea Birger found a gonococcal infection of Bartholin's glands in 18 per cent. Treatment is difficult as the ducts are too small to permit of any local treatment being carried out through them. The swollen gland may be punctured with a hypodermic syringe and a solution of nitrate of silver, albargin or other silver salt injected. This may be repeated at intervals but in many cases the only effective way to deal with the condition is to excise the infected portion of the gland.

Infection of the rectum occurs in about half the cases of adult female gonorrhoea and is not easily amenable to treatment. The symptoms are merely slight irritation with some purulent discharge, or they may be so slight as not to be noticed at all.

The treatment consists in trying to remove the gonococci and inflammatory exudation by irrigating the rectum with some mild antiseptic solution and then applying one of the silver salts, say 2 per cent. silver nitrate in solution or 5 per cent. albargin, by means of a swab passed through a speculum, to the whole surface of the

mucous membrane. Suppositories made up with Unna's paste mass and containing albargin, protargol or one of the silver salts may be inserted daily as long as the rectum will tolerate them.

CHAPTER VIII

GONOCOCCAL OPHTHALMIA

Gonococcal ophthalmia is usually described as a complication of gonorrhoea, and no doubt in most cases the patient is actually suffering from gonorrhoea and does convey the gonococci from the genital organs to his eyes, but the gonococci may equally well be derived from a focus in some other person, and the patient may quite possibly never have suffered from any gonococcal infection previously to acquiring the gonococcal ophthalmia. Hence we have placed this disease in the group of primary infections.

Incidence.—It occurs mostly in newly born infants and in young adults. In infants the disease is usually known as ophthalmia neonatorum, and the infection is contracted from the mother during parturition or within a few days of birth. In the young adult the infection is

usually conveyed from the genital organs, but it may also be transmitted on a towel which has been used to wipe away some gonococcal discharge. Medical men and nurses engaged in the treatment of patients having a gonococcal discharge may through carelessness infect their eyes.

Sypmtoms and Course.—The infection begins suddenly as an acute conjunctivitis. If the cause of this condition is not detected and no treatment is employed the progress of the disease is extremely rapid. In twenty-four hours or so the eyelids are enormously swollen, the conjunctivae intensely congested and a copious thick purulent secretion wells out from between the oedematous lids. In a very short time the vessels may become so congested as to lead to stasis of the circulation and destruction of the cornea.

Diagnosis.—This must be made by finding the gonococci in the secretion from the conjunctiva. In the earliest stage of the disease gonococci may be relatively scarce in the mucò-purulent discharge; hence when a sudden acute conjunctivitis occurs in a young adult a prolonged search should be made before coming to the

conclusion that the attack is not due to gonococcal infection. The gonococci soon become abundant and are easily found.

Prognosis.—This depends almost entirely on how far the disease has been allowed to progress before treatment is begun. If seen soon after the infection has taken place and vigorously treated the prognosis is good. If the disease has become firmly established before treatment is begun there is certain to be some permanent interference with the acuteness of vision, possibly total blindness or even loss of the eyeball. In the special institutions for the blind from one-third to one-fifth of all cases of blindness are attributed to gonococcal ophthalmia.

Prophylaxis.—In infants. By dropping a 2 per cent. solution of nitrate of silver into the eyes of each newly born child, Crédé reduced the incidence of ophthalmia neonatorum in the municipal hospital of Leipsic from 10 per cent. to less than 1 per cent. of all children born in the institution. This treatment unfortunately causes severe irritation in about one-third of the cases. Protargol in 5 per cent. solution, argyrol

in 10 per cent. solution, and many of the other newer organic compounds of silver are more efficient than the nitrate and cause much less irritation. Hörder states that by using sophol in 10 per cent. solution he had not a single case of ophthalmia, during the first five days of infant life, among 1,757 children born in municipal hospitals, and that among the whole of these children only seven showed definite signs of irritation.

Adults suffering from gonorrhoea or persons attending to cases of gonococcal infection should be instructed as to the danger of infecting the eyes by gonococcal pus conveyed on the fingers, instruments or articles of toilet. The necessity for disinfecting the fingers after handling any infective pus should be impressed on patients suffering from gonorrhoea.

Treatment.—This must be prompt and thorough if the vision is to be saved. Usually only one eye is affected, therefore the very first thing to do is to protect the other eye from infection by fixing a Buller's shield over it. This is merely a watch glass retained in position by a piece of

adhesive plaster. The section of the watch glass lying next to the angle formed by the nose and the eyebrow is very liable to work loose, and as this is the most dangerous area it must be frequently looked at to make certain that the plaster is in close contact with the skin. The actual treatment of the diseased eye must be carried out on the same general principles applicable to all gonococcal infections, i.e. the free gonococci, pus and toxin must be washed away as frequently as possible, while an endeavour is made to destroy the gonococci which have obtained a 'foothold in the tissues of the part. It must of course be borne in mind that the progress of the disease is very much more rapid in this situation than elsewhere, that the damage inflicted may be irreparable and that the part is exquisitely sensitive. The solution chosen for irrigation matters little provided the irrigation be done frequently and thoroughly. The eyelids should if possible be everted; if they are too much swollen to permit of this they must be gently lifted off the eyeball while the irrigation is being carried out so that the fluid may come in contact with every part of

the mucous membrane. The fluid should only be allowed to trickle in a gentle stream ; this may be accomplished by letting it run out of an ordinary glass syringe without pushing the piston, or if a freer flow is desired a small irrigating can and tube held practically on the level of the patient's head will be found useful.

Some people prefer perchloride of mercury 1 in 4,000, others select permanganate of potassium 1 in 10,000 or sterile salt solution. In severe cases the irrigation should be carried out every half-hour by day and every hour by night, the intervals being increased as the severity of the disease diminishes. After every irrigation a gonococcicidal agent should be employed. The most effective is nitrate of silver 5 grains to the ounce of distilled water. It causes intense pain, therefore some analgesic, e.g. a 2 per cent. solution of cocaine should be employed before applying the silver nitrate solution. Albargin 5 to 10 grains to the ounce, or argyrol of double this strength, are probably as effective and much less painful. Hegner (*Münch. Med. Wochen.* No. 32, 1911) has recently published some excellent

results obtained by using a 5 per cent. solution of syrgol (an albuminate of colloidal silver). Hörder (*Münch. Med. Woch.* No. 31, 1911) strongly recommends a 10 per cent. solution of sophol (a formonucleinate of silver). Whatever drug is selected success depends on the care which is taken to bring it into contact with every part of the conjunctiva. The margins of the lids should be smeared with vaseline to prevent them from adhering to each other and so retaining the discharge. A pad of absorbent wool moistened with boric lotion should be laid on the eye to absorb the discharge as it exudes from under the lids; this pad must be frequently renewed. Atropine should be instilled two or three times a day to prevent adhesions of the iris. If the treatment is begun before the cornea has become seriously involved the improvement is usually fairly rapid and there may be complete recovery with perfect vision.

If perforation of the iris has occurred treatment must be continued till the gonococcal infection has been got rid of and the case then turned over to the ophthalmic surgeon.

CHAPTER IX

GONOCOCCAL VULVO-VAGINITIS OF LITTLE GIRLS

THIS affection occurs much more commonly in young children than was up till recently supposed to be the case. A. Hamilton (*Journ of Infect. Diseases*, Vol. V., 1908) states that 4 per cent. of all applicants for admission to the Babies' Hospital, New York, were on examination found to be suffering from gonococcal vulvo-vaginitis. The infection is most commonly contracted from the mother, less often from the father or one of the other members of the family. The infection may be conveyed by the mother's fingers or on sponges or towels. In children's hospitals the disease is liable to occur in epidemic form and is then usually due to two or more children sharing the same bath or less often to

the careless use of clinical thermometers in the rectum. Chambers and the seats of water closets may also be the means of spreading the disease, for as long as a drop of infected pus remains moist the gonococci retain their virulence and the mucous membranes of female children are specially susceptible to invasion by this germ.

Girls over thirteen years of age usually escape infection and the great majority of cases occur in those under five years of age. Birger (*Archiv. Dermat. Syph.*, Band 106) in 151 cases of gonorrhoea among children under eleven years of age found gonococci in the following situations: Urethra, 151 = 100 per cent.; Vagina, 151 = 100 per cent.; Rectum, 79 = 53 per cent.; Bartholin's Glands 1 = 0·7 per cent. The symptoms are usually a muco-purulent discharge, which may be profuse or nearly absent, and the vulva is more or less inflamed and tender when touched.

Prognosis.—This is not very good. Birger found that 48 per cent. of the apparently cured cases relapsed. Just as in the case of adults any of the complications may occur and there is some evidence that the commencement of

menstruation may be delayed as a result of a gonococcal infection in childhood.

Prophylaxis.—To prevent its occurrence rules on the following lines should be drawn up and strictly adhered to.

Every child admitted for any disease whatever should be inspected, and if any suspicion of a vaginal discharge is noted the child must not be placed in a general ward with other children. The discharge, even if only a slight mucoid one, must be repeatedly examined till its cause has been definitely ascertained. In the meantime the child must be kept in an observation ward set apart for such cases and provided with separate water closets, baths and bed utensils. The day and night nurses doing duty in this ward must not be allowed to do anything for the children in the other wards. A special ward must be retained for children suffering from gonococcal vulvo-vaginitis. This ward must have separate nursing staff, lavatories, articles of toilet and linen; the nurses should be specially instructed as to the highly contagious nature of the disease. After attending to each child the nurse's hands should

be carefully disinfected, as otherwise a child which had almost recovered might be reinfected with a fresh strain of gonococci. The bath must also be scrubbed out with some antiseptic after each child is bathed. It would be much sounder to do away with the ordinary bath tub and only to use a shower bath. All bed utensils must be disinfected immediately after use. All towels and linen supplied for use in the ward should be specially marked, one set for each patient, and not used generally throughout the ward. A hot drying cupboard should be provided in which every towel or sheet should be thoroughly dried immediately after being used and before being sent to the laundry. Sponges should of course be prohibited, pieces of lint being used in their place, and these should be burnt as soon as finished with. It must be impressed on the staff that the gonococcus if allowed to remain in a moist condition will retain its vitality for twenty-four hours and that the vulva and vagina of little girls is extremely susceptible to infection with the gonococcus. If an epidemic is allowed to begin it is no easy matter to stamp it

out again. In an epidemic of this kind little boys usually escape infection.

Treatment.—As in all other forms of gonorrhoea cleanliness of the part is the first thing to be aimed at. This may be effected to a certain extent by hip baths, or better by gentle douching of the parts, using potassium permanganate 1 to 2 grains to the pint of warm water. The stream of solution must be allowed to run gently over the parts and great care must be exercised to prevent it from forcing the infection further into the vagina. After the douching the parts should be gently dried with a swab of absorbent material, which must be burnt immediately. If the parts are not too tender they should then be painted with a solution of nitrate of silver $\frac{1}{4}$ grain to the ounce of distilled water or albargin 1 to 2 per cent. Any excoriated patches should be smeared with some soothing ointment, e.g. zinc ointment and vaseline equal parts. A pad of absorbent antiseptic gauze should be constantly worn to intercept any discharge. Injections of gonococcal vaccine have yielded favourable results in many cases.

Birger found that the average time required for treatment of children with gonococcal infections was 80·4 days, although the actual time in different cases varied between 28 and 296 days.

CHAPTER X

GONOCOCCAL SEPTICAEMIA. ITS MANIFESTATIONS

Gonococcal septicaemia always arises from a pre-existing focus within the body. Gonococci have been cultivated from the blood of numerous cases in which the infection had spread by metastasis to parts distant from the original seat of infection. When this happens several different clinical manifestations may be shown. Thus there may be a definite septicaemic disease resembling typhoid fever. Dieulafoy (*Bull. de l'Académie de Méd.*, May 18, 1909) reported two such cases.

The commoner metastatic manifestations are arthritis, endocarditis, iritis, hyperkeratosis of the skin, phlebitis, arteritis, pleurisy and periosteal abscesses. The gonococcus in fact shows a

marked predilection for serous membranes and endothelium, much less so for other tissues.

Arthritis.—It is difficult to say how often this complication occurs, as few statistics are published on the subject. In a series of 812 cases, arthritis occurred 15 times = 1·7 per cent. Any joint in the body may be affected, those of the upper and lower extremity which are exposed to severe muscular strains are especially liable to be attacked, and the knee more often than any other joint.

Symptoms.—The patient has generally had gonorrhoea for some time when he suddenly complains of acute pain in one joint. In a few hours this joint becomes swollen and extremely painful. There is also more or less pyrexia and the patient feels distinctly ill. Within the next few days probably another, or sometimes several, joints are similarly affected, although the infection may remain limited to the original joint. The affected joints may remain swollen and painful, somewhat resembling the condition of an acute tuberculous joint, for weeks, while the temperature chart shows a moderate degree of

pyrexia. In other cases the joint may become steadily worse, shooting pains may occur at night, pointing to erosion of the articular cartilages. After a period of weeks, or even months, the joint may be full of fluid which if aspirated may be turbid or definitely purulent, and which may or may not contain gonococci.

The inflammation may clear up entirely, leaving a useful joint, but more commonly the termination of the attack is either that the ligaments are left permanently relaxed, and this is especially liable to occur in affections of the metatarsal joints, thus giving rise to flatfoot, or the plastic exudation thrown out may become organized into fibrous tissue leading to anchylosis of the joint.

TREATMENT.—In general the treatment is that of an inflamed joint, and as the joints of the lower extremity are generally more or less affected the patient should be kept in bed. The actual treatment adopted in any particular case should depend on the intensity of the inflammation.

If this is very acute and accompanied by pyrexia the joint should be immobilized and hot fomentations applied; mild extension also helps

to relieve the pain. The most effective remedy is gonococcal vaccine which should be injected as soon as possible and the dose repeated at intervals of a few days to a week, according to the reaction produced, till the symptoms have subsided.

The following case shows the value of the vaccine in what would undoubtedly have proved a very obstinate case if treated by pre-vaccine methods.

Boy N. 1st attack. Date of infection not known. He was admitted to hospital on December 21, 1908, with acute gonorrhoea and epididymitis. On December 29, 1908, he suddenly developed pyrexia, the temperature rising to 104° F., and acute arthritis of the elbow joint. The usual treatment was tried for a fortnight but without effecting any improvement. On January 13, 1909, a supply of gonococcal vaccine having been received, he was given an injection containing 200 million gonococci. Next day there was a marked improvement in all his symptoms. A second injection was given ten days after the first, following which all his symptoms cleared up and he was discharged hospital, apparently cured,

on February 9, 1909, twenty-six days after receiving the first injection. Considering the patient's youth and the severity of his symptoms the result in this case may be regarded as extremely satisfactory.

In subacute cases with mild pyrexia the patient should be put to bed. Gonococcal vaccine should be given, but if the affection has existed for some time the results may be disappointing. In addition to keeping the joint at rest counter-irritants should be freely employed. When the inflammation is of mild degree Bier's congestion treatment followed by vigorous massage is often most beneficial.

In the old chronic case with no pyrexia and in which the ligaments have either become relaxed or thickened, with probably also some adhesions of the joint surfaces, vaccines are of little use and the treatment must be conducted on purely surgical lines.

Hildebrand (*Berlin. Klin. Wochen.*, No. 31, 1911) recommends that the joint should be punctured and 5 gm. of tincture of iodine injected into it. He says that this gives rise to some pyrexia

but never to anchylosis, and thinks that the iodine not only kills any gonococci free in the joint but that it also penetrates the tissues and kills off any cocci embedded in them.

Gennerich of Kiel speaks very highly of the effect of irrigating the inflamed joint with 1 per cent. solution of collargol.

One important fact to remember is that a joint which has become severely infected with gonococci requires some time to allow of its ligaments regaining their normal elasticity. It is especially to joints of the lower extremity, and more particularly those of the metatarsus that this applies. When these patients are allowed to get up and walk about as soon as the process has somewhat subsided the ligaments, and probably also the plantar fascia, become stretched and give way with the result that the patient acquires a flatfoot for the rest of his life.

Closely allied to gonococcal arthritis is gonococcal tenosynovitis. The tendons around the wrist joint and ankle are those most often affected, probably because they are subjected to severe mechanical strain. The

symptoms are the usual ones of acute inflammation commencing suddenly and accompanied by considerable swelling and pain. The condition tends to become subacute or chronic and to persist for a considerable time; it may simulate a tuberculous infection.

TREATMENT.—When the condition is acute the part should be kept at rest and hot fomentations applied; when the inflammation has subsided counter-irritants may be employed; Bier's congestion treatment followed by massage may often hasten resolution. Injections of gonococcal vaccine should if possible always be tried. In one of our cases a subacute inflammation of the tendons around the wrist joint, which had failed to respond to treatment, completely cleared up in a fortnight when injections of gonococcal vaccine were given.

Affections of the Skin Due to Gonococci.—Buschke classifies these as: Simple erythema; Urticaria; Erythema nodosum; Haemorrhagic and bullous exanthems; Hyperkeratosis.

The skin affections do not occur very frequently in the course of gonococcal infections and it is

only the hyperkeratoses which are worth mentioning.

These affections have attracted a good deal of attention lately. Meyer and Arning (*Arch. Derm. u. Syph.*, Bd. cviii., Heft 1 and 2) and Rost (*Derm. Zeitschr.*, March, 1911) have contributed some good papers on this subject. Gonococcal hyperkeratosis nearly always occurs in conjunction with gonococcal arthritis which has been in evidence for some time. The affection occurs on the glans penis, where it is also described as balanitis circinata, and on the soles of the feet and palms of the hands. It may begin as a pustular eruption or a red patch; in a few days the redness fades and the pustule dries up, leaving a slightly raised indurated patch consisting of heaped-up transparent yellowish horny layers of epithelium. These patches may be so close together as nearly to cover the soles of the feet and palms of the hands. Gonococci have not so far been cultivated from the exudation or patches. The treatment should be directed to the original focus of infection and to the arthritis.

Gonococcal Iritis.—Iritis not infrequently

occurs in persons who have had an attack of gonorrhoea and believe themselves to be cured. Whether the iritis is due to the presence of actual gonococci or merely to their toxin is not at present definitely known and is indeed of small importance.

The iritis usually comes on some time, i.e. months or years after the gonorrhoea has been apparently cured. Generally only one eye is attacked; it is extremely painful and the conjunctiva is more than usually congested. The iritis is very persistent and liable to relapses. Men suffer much more frequently than women. Many of the so-called cases of rheumatic iritis are in all probability really of gonococcal origin.

The treatment is that of iritis. Injections of gonococcal vaccine can do no harm and might prove most beneficial.

Endocarditis and Pericarditis.—When gonococci gain admission to the general blood stream they may set up an inflammation of any of the blood-vessels or cavities lined with endothelium. The literature on this subject is not at present very voluminous but a certain number of cases

have been published. Gonococcal arthritis is usually present when one of the serous cavities is attacked.

The aortic valve is more frequently attacked than the others, probably because of the greater strain thrown on it. The patient usually looks and feels ill, there is considerable pyrexia and on examination a bruit of variable character may be heard over the affected valve. In addition to adopting measures to save the heart from all unnecessary strain the only hope of averting serious damage to the valve, if not indeed a fatal issue, lies in the administration of gonococcal vaccine.

Inflammation of the walls of arteries and veins has been ascribed to gonococci and no doubt does occur, but it is not always easy to prove the presence of the causal germs, while beyond the injection of gonococcal vaccine there is no special treatment indicated.

Periosteal abscess due to gonococci is of rare occurrence and presents no special features; it is only when the pus is examined bacteriologically that the true cause of the affection is recognized.

APPENDIX

FORMULÆ FOR USE IN GONORRHOEA

For Injection

1. Potasssium permanganate . . 1 grain
   Distilled water . . . . 1 oz.

One to two teaspoonfuls to a wineglass of warm water.

2. Protargol . . . . . 4 grains
   Water . . . . . 1 oz.

Dissolve the protargol in cold water. Use one part of the solution with three of water at first, gradually reduce the proportion of water till the plain solution is being used.

3. Oxycyanate of Mercury . . . 1 part
   Water . . . . . 1,500 parts

Mix with an equal quantity of warm water.

4. Zinc sulphate and zinc sulpho-carbolate of each . . . . 1 grain
   Water . . . . . 1 oz.

For Irrigation

1. Potassium permanganate . . 20 grains
   Distilled water . . . . 20 oz.
2. Albargin . . . . . 50 grains
   Distilled water . . . . 20 oz.
3. Nitrate of silver . . . . 20 grains
   Distilled water . . . . 20 oz.
4. Sulphate of zinc . . . . 50 grains
   Water . . . . . 20 oz.

One to two ounces to each pint.

STAINS AND CULTURE MEDIA REFERRED TO, BUT NOT DESCRIBED IN THE TEXT

STAIN MIXTURES

PAPPENHEIM'S STAIN (Krsztalowicz' modification).

Methyl Green	0·15
Alcohol	2·5
Pyronin	0·25
Glycerine	20·0
Sol. Acid. Carbolic (2 per cent.) ad	100·0

Allow to act for twenty to thirty seconds; wash with water; dry with blotting paper.

Cocci stain purple red, protoplasm of cells, rose-red, nuclei, blue-green.

LESZCZYNSKY'S STAIN

Stain for one minute in the following mixture:—

Saturated watery solution of thionin-blue	10·0
Acid. Carbolic	2·0
Distilled water	88·0

Wash with water and stain for one minute in

Saturated watery solution of picric acid
Solution of potassium hydrate (0·1 per cent.) } equal parts

Wash with water, dry with blotting paper, treat with absolute alcohol for five seconds, wash again with water, dry and examine.

Intracellular cocci stain black, but not extracellular.

Most other bacteria found in urine stain yellow-red to red.

LANZ'S STAIN

Saturated solution of thionin-blue in 2 per cent. carbolic	4·0
Saturated solution of fuchsin in 2 per cent. carbolic	1·0

Mix immediately before use and allow to act for fifteen to thirty seconds. Cocci stain blue; nuclei of cells, bluish red; and their protoplasm, light red.

For studying the cytology of pus a suitable blood stain should be used, of which the following is recommended:

LEISHMAN'S STAIN

Leishman's stain in powder . . .	0·15
Methyl alcohol (Merck's pro analysi, acetone free)	100·0

Grind the stain to a fine powder in a clean mortar; add a few c.c. of the alcohol and grind well to make a paste; slowly add more alcohol, while grinding, till about 15 c.c. have been added. Allow to stand for a few minutes to let the undissolved stain settle to the bottom; decant into a clean drop bottle and repeat the process with the remainder of the solid stain in the mortar. Continue till all the powder and alcohol have been transferred to the bottle. It is best to keep the prepared stain for three days, with frequent shaking, before using it.

Allow the specimen to dry in air and, without fixing it, drop sufficient of the prepared stain on it to cover it completely; allow the stain to act for fifteen to thirty seconds and then add to it as many drops of distilled water as were used of the stain. Mix stain and water well by drawing a needle through them from end to end of the slide two or three times; allow the diluted stain to act for five to ten minutes and then wash with distilled water. Leave some of the latter on the slide for fifteen to thirty seconds, wash off and dry with blotting paper. Cocci stain blue; nuclei of leucocytes, rose-red; eosinophile granules, red; protoplasm of mononuclear and coarsely grained eosinophile cells, light blue.

LEITH MURRAY'S DILUTING FLUID (for standardization of vaccines)

Giemsa's stain	10·0 c.c.
Sodium Chloride	0·1 grm.
Formalin	4·0 c.c.
Distilled water to	100·0 c.c.

CULTURE MEDIA

Wassermann's Pig-serum Nutrose Medium

Place in an Erlenmeyer flask 15 c.c. of pig-serum, as free from haemoglobin as possible, and add to it 30 to 35 c.c. of distilled water, 2 to 3 c.c. of glycerine and 0·8 to 0·9 grm. of nutrose. Shake well and heat over an open flame, while shaking, till the mixture becomes clear. Sterilize in a steamer.

For use, warm the mixture to 50°C. and add one part of it to one of 2 per cent. nutrient agar which has been melted and cooled to the same temperature. The medium must not be boiled after the agar has been added or the albumin in it will coagulate.

Finger's Urine Agar

Nutrient agar (2 per cent.)	2
Sterile urine	1

The above are useful substitutes for the less easily obtained human serum agar, after the gonococcus has been subcultured for some generations on the latter medium.

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